MARCH, 1949

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

SYMPOSIUM ON METABOLISM, NUTRITION AND ALLERGY

Amino Acids in the Production of Plasma Protein and Nitrogen Balance

Endocrine Disturbances in Gastrointestinal Conditions

Allergy As a Factor in Gastrointestinal Disorders

Nutritional Therapy: Some Facts and Problems

●

Fourteenth Annual Convention

Boston, Mass., 24, 25, 26 October 1949

VOLUME 16 NUMBER 3

The most potent androgen...

PERANDREN

(testosterone propionate U.S.P. XIII)

IN THE MALE "The principal usefulness . . . has been as a replacement therapy . . ."[1] when functional or organic testicular deficiency exists.

The chief indications are the male climacteric, hypogonadism, and impotence due to glandular causes.

Dosage is from 10 to 25 mg. one to three times a week. Perandren should be discontinued or the dose decreased if priapism supervenes, or if mental excitement occurs. The amount administered to prepuberal boys should be insufficient to precipitate puberty.

IN THE FEMALE "... the use of androgens in women has resulted in . . . more effective management of a variety of clinical disorders."[2]

These include the menopausal syndrome, functional uterine bleeding and dysmenorrhea.

Dosage should not exceed 300 mg. per month. Perandren should be discontinued or the dose decreased if signs of masculinization appear.

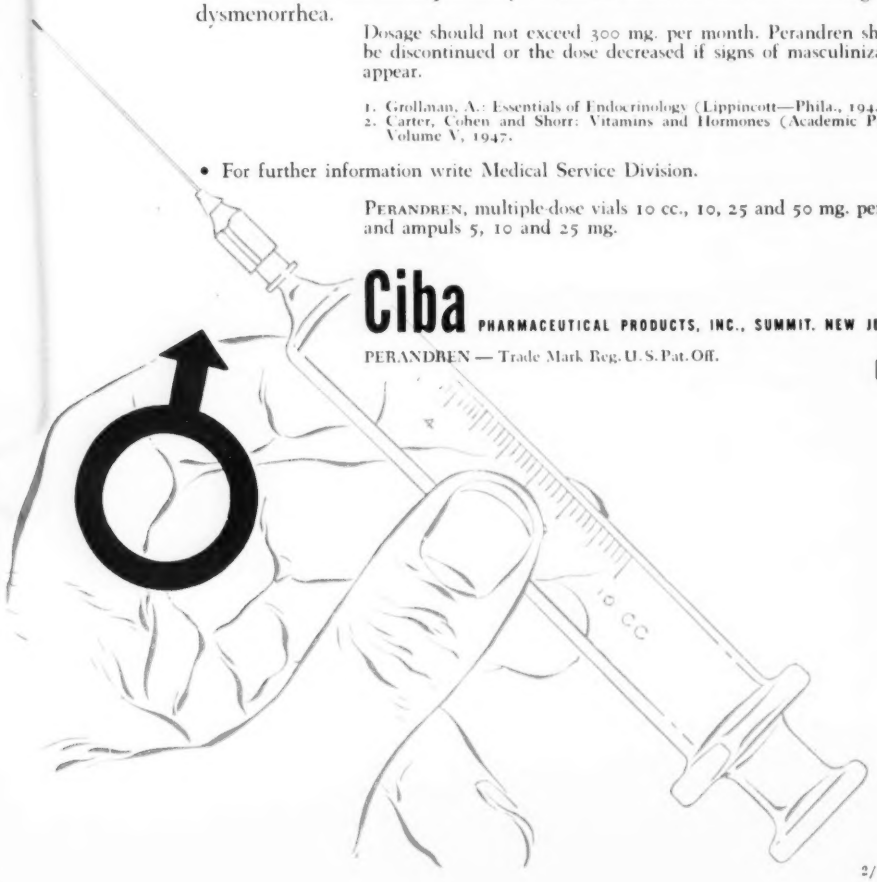
1. Grollman, A.: Essentials of Endocrinology (Lippincott—Phila., 1944).
2. Carter, Cohen and Shorr: Vitamins and Hormones (Academic Press), Volume V, 1947.

• For further information write Medical Service Division.

PERANDREN, multiple-dose vials 10 cc., 10, 25 and 50 mg. per cc., and ampuls 5, 10 and 25 mg.

Ciba PHARMACEUTICAL PRODUCTS, INC., SUMMIT, NEW JERSEY

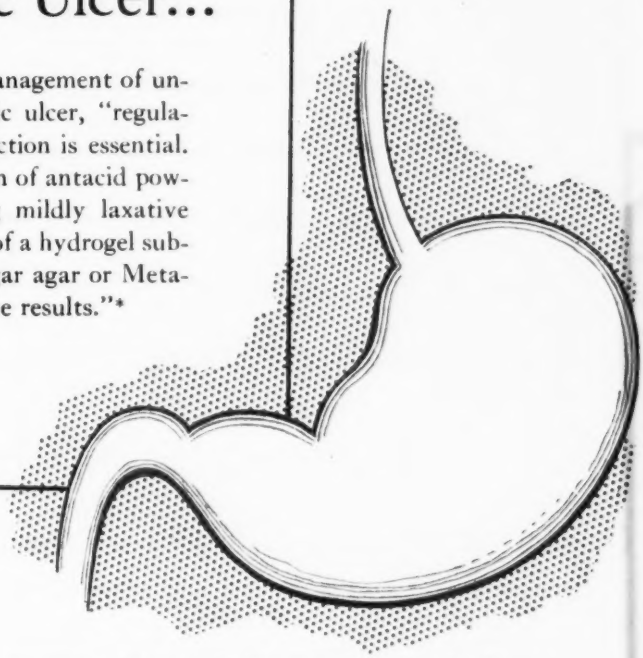
PERANDREN — Trade Mark Reg. U.S. Pat. Off.



2/1110M

Bowel Regulation in Peptic Ulcer...

In the medical management of uncomplicated peptic ulcer, "regulation of bowel function is essential. . . . A combination of antacid powders . . . having mildly laxative effects or the use of a hydrogel substance, such as agar agar or Metamucil, will produce results."*



By furnishing a water-retaining, gelatinous residue in the large bowel, Metamucil acts gently without irritation to promote smooth, normal evacuation.

METAMUCIL®

is the highly refined mucilloid of Plantago ovata (50%), a seed of the psyllium group, combined with dextrose (50%) as a dispersing agent.

ACCEPTED COUNCIL ON PHARMACY AND CHEMISTRY AMERICAN MEDICAL ASSOCIATION

SEARLE RESEARCH IN THE SERVICE OF MEDICINE

*Gerendasy, J.: Modern Treatment of Peptic Ulcer, J. M. Soc. New Jersey *43*:84 (March) 1946.

In Chronic Cholecystitis...

First & Foremost chemically pure bile acid derivative made available for therapy, Council-Accepted since 1932, exhaustively studied and most favorably reported by hundreds of investigators, Decholin® remains today a bile acid preparation for use in the medical management of chronic cholecystitis.

The Most Potent Hydrocholeretic,

Decholin multiplies and frees the flow of thinned liver bile. By thus easing biliary evacuation and closely simulating a physiologic drainage of accumulated foreign matter through the hepatic and common ducts, Decholin may lessen the epigastric and right upper quadrant discomfort typical of chronic cholecystitis, improve the patient's tolerance for food and reduce the periods of disability.

Decholin

dehydrocholic acid

3¾ gr. tablets in bottles of 25, 100, 500, and 1000.

Decholin Sodium® (sodium dehydrocholate) in 20% aqueous solution; ampuls of 3 cc., 5 cc. and 10 cc., packages of 3 and 20 ampuls.

The Fifth Edition of "Decholin in Biliary Tract Disturbances" is now available upon request.

AMES

AMES COMPANY, INC.
ELKHART, INDIANA

The REVIEW *of* GASTROENTEROLOGY

(INCORPORATING THE AMERICAN JOURNAL OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

VOLUME 16 MARCH, 1949 NUMBER 3

CONTENTS

Page

Editorial Board 198
General Information 200
Symposium on Metabolism, Nutrition and Allergy:
Allergy As a Factor in Gastrointestinal Disorders ..... *Louis Tuft, M.D.* 209
Amino Acids in the Production of Plasma Protein and Nitrogen Balance *S. C. Madden, M.D.* 218
Endocrine Disturbances in Gastrointestinal Disturbances *Morton S. Biskind, M.D.* 220
Nutritional Therapy: Some Facts and Problems *Herbert T. Kelly, M.D., F.A.C.P.* 226
Urethane Therapy in Leukemia *Adolph J. Creskoff, M.D. and Thomas Fitz-Hugh, Jr., M.D.* 243
Recent Advances in Physical Medicine ..... *Richard Kovacs, M.D.* 250
The Effect of Urine Extract from Oöphorectomized Dogs on Gastric Secretion *Jerzy Kaulberz, Ph.D., M.D.; Thomas L. Patterson, Ph.D., Sc.D.; David J. Sandweiss, M.D. and Harry C. Saltzstein, M.D.* 254
The Effect of Urine Extract from Thyroidectomized Dogs on Gastric Secretion *Jerzy Kaulberz, Ph.D., M.D.; Thomas L. Patterson, Ph.D., Sc.D.; David J. Sandweiss, M.D. and Harry C. Saltzstein, M.D.* 257
Editorials:
The Surgery of Portal Obstruction and Portal Hypertension *A. O. Wilensky, M.D.* 260
The Fifteenth Anniversary of THE REVIEW OF GASTROENTEROLOGY *Samuel Weiss, M.D., Sc.D., F.A.C.P.* 261
Chapter Activities 263
News Notes 264
In Memoriam 264
Abstracts 265
Book Reviews 268

Owned and published monthly by the National Gastroenterological Association, Inc. Editorial Office: 146 Central Park West, New York 23, N. Y. Business Office: 1819 Broadway, New York 23, N. Y. Copyright, 1949, by the National Gastroenterological Association, Inc. Subscription rate, U. S., Pan-American Union: One year $5.00, two years $9.00 (foreign $7.00, $13.00) Single copy: $.50. *Reentered as second class matter, February 24, 1947, at the Post Office at New York, N. Y., under the act of March 3, 1879.*

Index to Advertisers

Ames Co., Inc. 196
Bischoff, Ernst, Co., Inc. 275
Carel Laboratories 202
Ciba Pharmaceutical Products, Inc. ..... 2nd Cover
Coca-Cola Co. 262
Eaton Laboratories, Inc. 206
Eder Instrument Co. 272
Endo Products, Inc. 280
Hoffmann-La Roche, Inc. 208
Knox Gelatine 276
Lannett Co., Inc., The 274
National Drug Co., The 207
Parke, Davis & Co. 201
Reynolds, R. J., Tobacco Co. 199
Robins, A. H., Co., Inc. 203, 204
Pystan Co., Inc. 273
Sandoz Chemical Works 271
Schering Corp. 277
Searle, G. D., & Co. 195
Standard Pharmaceutical Co., Inc. 259
Swift & Co. 278
Van Patten Pharmaceutical Co. 279
Warner, Wm. R. ..... 3rd Cover
Winthrop-Stearns, Inc. 205
Wyeth, Inc. ..... 4th Cover

The Review of Gastroenterology

OFFICIAL PUBLICATION

of the

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

1819 Broadway, New York 23, N. Y.

Editorial Office, 146 Central Park West, New York 23, N. Y.

SAMUEL WEISS, *Editor*

EDITORIAL BOARD

ANTHONY BASSLER — HARRY M. EBERHARD

WILLIAM W. LERMANN

EDITORIAL COUNCIL

F. W. BANCROFT
W. A. BASTEDO
RICHARD BAUER
BENJAMIN M. BERNSTEIN
THEODORE BLUM
DONOVAN C. BROWNE
JOSE OVIEDO BUSTOS
JOHN CARROLL
LOUIS H. CLERF
F. J. CONLAN
FRANK A. CUMMINGS
FELIX CUNHA
RUDOLF R. EHRMANN
MAX EINHORN
HYMAN I. GOLDSTEIN
CHEVALIER L. JACKSON
WM. C. JACOBSON
I. R. JANKELSON
SIGURD W. JOHNSEN
ELIHU KATZ
RICHARD KOVACS
FRANZ J. LUST
G. RANDOLPH MANNING
CHARLES W. McCLURE
GEORGE G. ORNSTEIN
GEORGE T. PACK
GEORGE E. PFAHLER
A. SUMNER PRICE
HENRY A. RAFSKY
MARTIN E. REHFUSS
DAVID J. SANDWEISS
JOSEPH SCHROFF
MARKS S. SHAINE
I. SNAPPER
HORACE W. SOPER
WILLIAM H. STEWART
J. E. THOMAS
MAX THOREK
C. J. TIDMARSH
GABRIEL TUCKER
CARLOS BONORINO UDAONDO
ROY UPHAM
R. H. VOSS
MICHAEL WEINGARTEN
LESTER R. WHITAKER
FRANK C. YEOMANS

ABSTRACT STAFF

MARK S. SHAINE, *Chairman*

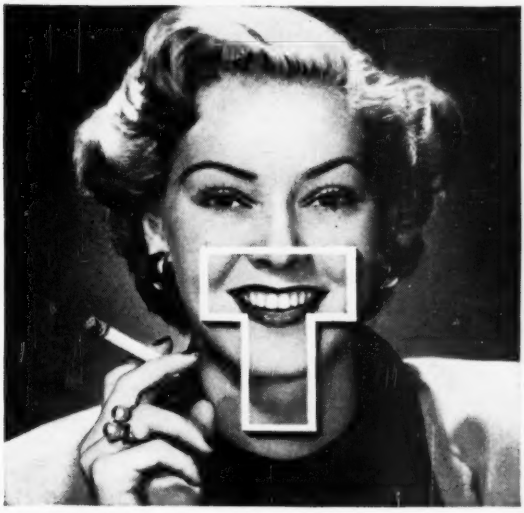
LESTER L. BOWER
A. J. BRENNER
JOHN E. COX
LEROY B. DUGGAN
WILLIAM E. FITCH
RICHARD I. KILSTEIN
ARTHUR A. KIRCHNER
WILLIAM LIEBERMAN
LIONEL MARKS
JACOB L. MATHESHEIMER
LOUIS K. MORGANSTEIN
WILLIAM L. PALAZZO
JACOB A. RIESE
H. M. ROBINSON
A. X. ROSSIEN
A. SLANGER
REGINALD B. WEILER

Business Office, 1819 Broadway, New York 23, N. Y.

DANIEL WEISS, *Managing Editor*

STEVEN K. HERLITZ *Advertising Manager*

How mild can a cigarette be?



In a recent coast-to-coast test, hundreds of men and women smoked Camels — and only Camels — for 30 consecutive days. These people smoked on the average of one to two packages of Camels a day during the entire test period. Each week, throat specialists examined these Camel smokers. A total of 2,470 careful examinations were made by these doctors. After studying the results of the weekly examinations, these throat specialists reported:

"NOT ONE SINGLE CASE OF THROAT IRRITATION DUE TO SMOKING CAMELS!"

Money-Back Guarantee!

Test Camel mildness for yourself in your own "T-Zone." T for taste, T for throat. If, at any time, you are not convinced that Camels are the mildest cigarette you've ever smoked, return the package with the unused Camels and we will refund its full purchase price, plus postage. *(Signed)* R. J. Reynolds Tobacco Company, Winston-Salem, North Carolina.

According to a recent Nationwide survey:

MORE DOCTORS SMOKE CAMELS

than any other cigarette

Doctors smoke for pleasure, too! And when three leading independent research organizations asked 113,597 doctors what cigarette they smoked, the brand named most was Camel!

GENERAL INFORMATION

Contributions: Articles are accepted for publication on condition that they are contributed solely to THE REVIEW OF GASTROENTEROLOGY.

Manuscripts should be typewritten double-spaced and the original copy submitted. Footnotes and bibliographies should conform to the style recommended by the American Medical Association.

Illustrations and diagrams should carry suitable lettering and explanations. Four illustrations per article are allowed without cost to the author.

News items of interest will receive due consideration.

REVIEWS: THE REVIEW OF GASTROENTEROLOGY will review monographs and books dealing with gastroenterology or allied subjects. It may be impossible to review all material sent. However, an acknowledgement will be made in the Department of Reviews.

The editors and publishers are not responsible for individual opinions expressed by their contributors, much less those given under current literature.

Reprints: A price list and order blank for reprints will be sent to each contributor before the journal is issued.

Manuscripts, abstracts, books for review and news items are to be sent to the Editorial office, 146 Central Park West, New York 23, N. Y.

Communications regarding business matters, advertising, subscriptions and reprints should be sent to the Business office, 1819 Broadway, New York 23, N. Y.

Subscription price: U.S. and Pan-American Postal Union: one year, $5.00, two years, $9.00. Elsewhere, $7.00, $13.00. Single copy $.50. Members of the National Gastroenterological Association receive the REVIEW as part of their membership.

Change of Address: Notify publishers promptly of change of address. Notices should be given both old and new addresses.

what's in a name ABDEC® kapseals®

ABDEC means comprehensive vitamin medication. The name signifies exactly and concisely a distinctive preparation providing vitamin *A*, the *B*-group, vitamin *D*, vitamin *E* and vitamin *C*—nine vitamins in all.

To the physician, **ABDEC** readily identifies a prophylactic and therapeutic agent of choice for promoting optimal nutritional status. Since deficiency states rarely involve but one vitamin, integrated multivitamin therapy with **ABDEC KAPSEALS** fosters a more satisfactory clinical response.

ABDEC KAPSEALS on your prescription affords the full benefits of comprehensive vitamin therapy to your patients.

DOSAGE: For the average patient, one ABDEC KAPSEAL daily; during pregnancy and lactation, two Kapseals daily. Three Kapseals daily are suggested in febrile illnesses, for preoperative and postoperative patients, and in other conditions in which deficiencies are likely to occur.

EACH ABDEC KAPSEAL CONTAINS

Vitamin A	5,000 U.S.P. units
Vitamin D	1,000 U.S.P. units
Mixed Tocopherols (Vitamin E factors)	5 mg.
Vitamin B_1 (Thiamine Hydrochloride)	5 mg.
Vitamin B_2 (Riboflavin)	3 mg.
Vitamin B_6 (Pyridoxine Hydrochloride)	1.5 mg.
Pantothenic Acid (As the sodium salt)	5 mg.
Nicotinamide	25 mg.
Vitamin C (Ascorbic Acid)	75 mg.

PARKE, DAVIS & COMPANY · DETROIT 32, MICHIGAN

MEDICAMENTA VERA · P D & CO.

Doctor:

If we should offer you the non selective germicide carbolic acid, shorn of its organotropic activity, yet accented as to parasitotropic power, would you not instantly discern a highly efficient chemotherapeutic agent?

We cannot so modify that basic Phenol but we do offer a higher Phenol, a more efficient microbicide, of non selective utility and devoid of discernible toxicity or adverse sequential symptoms.

This product is essentially a glyceryl ester of Alpha Naphthol in an excess of glycerol and saponified oils.

Recently a New York State physician wrote: "*Alpha Naphco* is the remedy of choice in treatment of intestinal 'flu' and Histamine cephalagia. This after twelve years and hundreds of patients." He further stated: "If I were allowed only one medication I would select *Alpha Naphco*."

A Seattle, Washington physician stated: "I've been using *Alpha Naphco* steadily during the past seven years in the treatment of allergy and I found it to be a very effective remedy for changing the intestinal flora from a putrefactive to an aciduric type. The success of my treatment is quite outstanding and at times almost dramatic."

(Names and addresses of above M.D.'s on request.)

Samples of liquid Alpha Naphco in adequate quantity available to any physician.

Alpha Naphco

NON-SELECTIVE

GERMICIDE

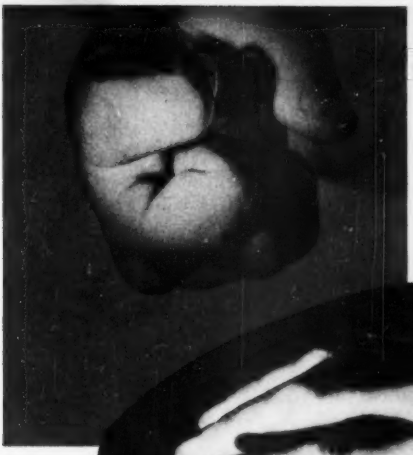
devoid of toxication

•

Literature and Samples on request.

Carel Laboratories

REDONDO BEACH • CALIFORNIA



relax the grip of spasm

The secret of Donnatal Elixir's unusual spasmolytic efficacy lies in its precise balance of the principal *natural* alkaloids of belladonna, plus its minimal content of phenobarbital • By blocking smooth muscle response to cholinergic nerve impulses, these alkaloids act synergetically to break the links of spastic reaction; and the sedative ingredient helps allay any psychogenic component • Controlled clinical studies—plus broad professional experience—attest its value in gastro-intestinal, biliary, urogenital, respiratory, or central nervous spasm.

for both somatogenic and psychogenic cases

for spasmolysis plus... sedation without toxicity

donnatal elixir

Also available as Donnatal Tablets and Donnatal Capsules

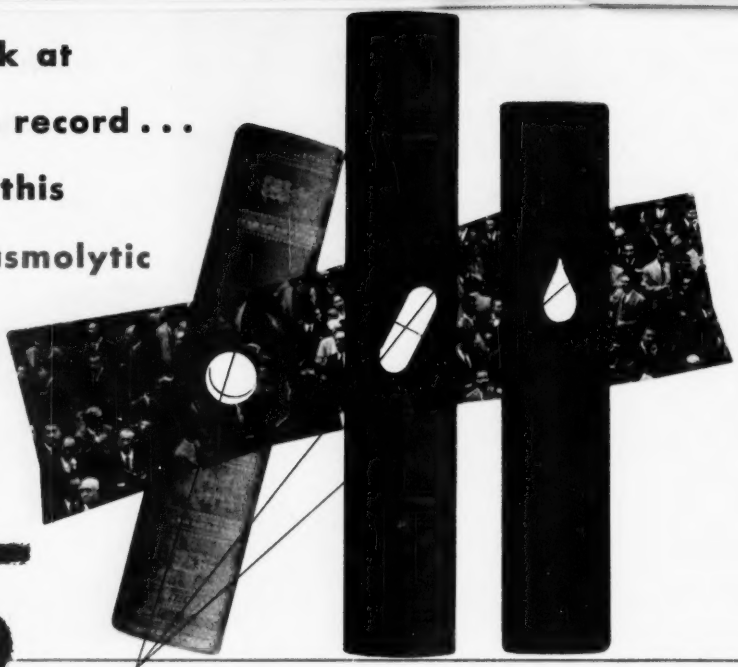
Robins

Each 5cc of donnatal elixir contains:

Hyoscyamine Sulfate	0.1037 mg.
Atropine Sulfate	0.0194 mg.
Hyoscine Hydrobromide	0.0065 mg.
Phenobarbital (1/6 gr.)	16.2 mg.

A. H. Robins Co., inc. **Richmond 20, Va.** ETHICAL PHARMACEUTICALS OF MERIT SINCE 1878

look at the record . . . on this spasmolytic



"A most effective therapy in the relief of pain and spasm"[2] . . . "more effective than either atropine or belladonna . . . [or] the synthetic[s]"[1] . . . "definite mitigation of pain"[3] . . . "Donnatal . . . may be given over a long period of time without any ill-effects or habit-formation"[1] • These conclusions from controlled clinical studies on Donnatal are a matter of published record: they reflect the wide professional acceptance of this superior spasmolytic.

Each tablet, capsule, or 5 cc. of elixir contains:

Hyoscyamine Sulfate	**0.1037 mg.**
Atropine Sulfate	**0.0194 mg.**
Hyoscine Hydrobromide	**0.0065 mg.**
Phenobarbital (¼ gr.)	**16.2 mg.**

A. H. Robins Co., Inc. Richmond 20, Va.

1. Kilstein, R. L.: Rev. Gastroenterol., 14:171, 1947.
2. Merrissey, J. H.: J. Urol., 57:635, 1947.
3. Ricci, J. V.: In The City Hospital Year Book, 1946, New York, 1947.

donnatal

tablets • capsules • elixir

natural
belladonna alkaloids
in natural
in spasmolysis

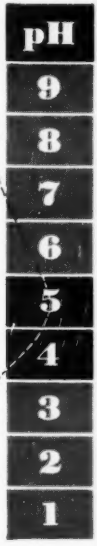
Robins

ETHICAL PHARMACEUTICALS OF MERIT SINCE 1878

"safety zone"

therapy of

PEPTIC ULCER



The gastric pH range which is safe for the peptic ulcer patient lies between 4 and 5. In this "safety zone" there is neither pepsin activity (which may cause continued erosion or bleeding) nor stimulation of excess acid production.

Tricreamalate, a balanced blend of aluminum hydroxide gel with magnesium trisilicate reduces acidity within the stomach to pH 4 to 5. Absolute neutrality is not reached. Hence, there is no stimulus to "acid rebound" and no alkalosis.

Through the formation of a protective coating and a mild astringent effect, nonabsorbable Tricreamalate is soothing to the irritated gastric mucosa, relieves gastric pain and heartburn, and aids in healing peptic ulceration as well as in preventing recurrence.

Tricreamalate

Aluminum Hydroxide Gel with Magnesium Trisilicate

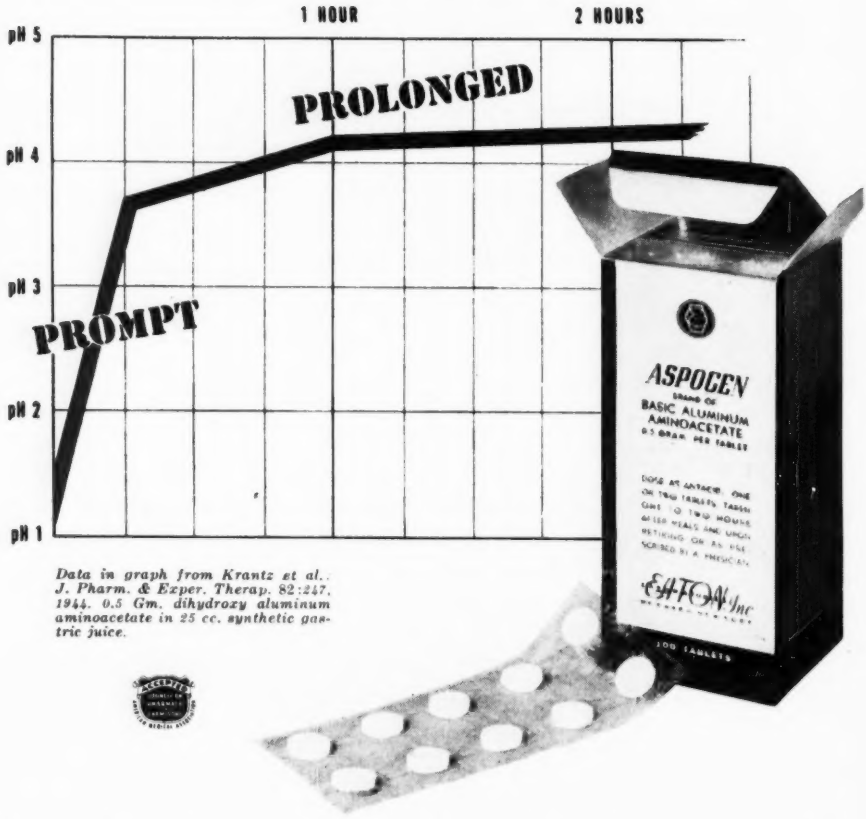
LIQUID
Bottles of 12 fl. oz.
TABLETS
Tins of 12
Bottles of 100 and 500

Dose: 1 or 2 teaspoonfuls or tablets every 2 to 4 hours.

Tricreamalate, trademark

Winthrop-Stearns INC.
NEW YORK 13, N. Y. WINDSOR, ONT.

Aspogen for peptic ulcer



Data in graph from Krantz et al., J. Pharm. & Exper. Therap. 82:247, 1944. 0.5 Gm. dihydroxy aluminum aminoacetate in 25 cc. synthetic gastric juice.

This new basic aluminum salt of the amino acid glycine has demonstrated its effectiveness as an adjunct in the treatment of peptic ulcer in several clinical studies.* It produced satisfactory results in 42 of one group of 44 patients and gave moderate to marked relief from pain to 81% of another group. Its freedom from objectionable side effects was well shown in the case of one patient, who, through misunderstanding, took 0.5 Gm. of this drug *hourly for eight days* without any ill effects. Aspogen® brand of dihydroxy aluminum aminoacetate N.N.R. is indicated in the treatment of peptic ulcer and for symptoms of hyperchlorhydria. It is available as soft, palatable 0.5 Gm. tablets sealed in cellophane in cartons of 100 or in bulk in bottles of 500. *Literature on request.*

Endocet
Experientia

EATON LABORATORIES, INC., NORWICH, N. Y.

*Krantz, J. et al.: J. Pharmacol. & Exper. Therap. 82:247, 1944 • Paul, W. et al.: J. Iowa M. Soc. 35:167, 1945 • Weisberg, J. et al.: Am. J. Digest. Dis. 15:332, 1948.

Transports hydrochloric acid and pepsin from the stomach.

Releases these agents in the proper environment for inactivation of pepsin and harmless neutralization of hydrochloric acid.

Effects prompt symptomatic relief.

Healing of the ulcer crater occurs "much more rapidly...than...with aluminum preparations."[1]

ACTION WITHOUT REACTION

Completely nontoxic anion exchange resin; chemically inert, insoluble and nonirritating.

Cannot produce alkalosis or acid rebound.

Does not remove chloride or phosphate ions.

Unlike magnesium or aluminum preparations, has no effect on the bowel.

RESINAT

Completely nontoxic anion exchange resin

FOR PEPTIC ULCER

RESINAT PATENT PENDING

Supplied:

Resinat Capsules (0.25 Gm.)
50's, 100's, 500's and 1,000's.

Resinat Powder (1 Gm. packets)
50's and 100's.

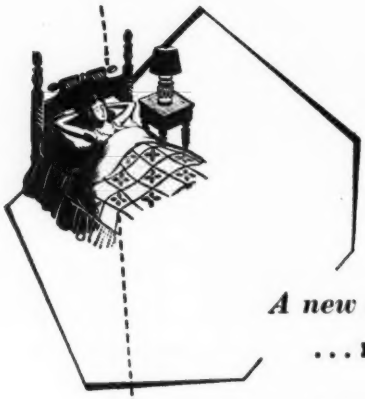
Dosage: 0.5 Gm. to 1 Gm. every 2 hours while awake. Following x-ray regression of the ulcer crater (usually 10-14 days)[1] dosage may be gradually reduced to a maintenance level; 0.5 Gm. 1 hour after meals and at bedtime.

1. Weiss, J.: Review of Gastroent., 15:826, Nov., 1948.

THE NATIONAL DRUG COMPANY, PHILADELPHIA 44, PA.

Manufacturers of

Pharmaceutical, Biological and Biochemical Products for the Medical Profession



A new sedative-hypnotic
... not a barbiturate

Presidon, the new, quick-acting, mild sedative hypnotic, is particularly well suited to the needs of tense and nervous patients with functional and organic disturbances of the gastrointestinal tract. It is a pyridine derivative, chemically different from the barbiturates, bromides and ureides. Therapeutically it differs in the low incidence of by-effects. Needed relaxation and sleep can be secured for patients with gastrointestinal disorders. Presidon is supplied in 0.2 Gm tablets, bottles of 20 and 100.

HOFFMANN-LA ROCHE INC. • NUTLEY 10 • N. J.

Presidon
T.M.—Presidon

'Roche'

The Review of Gastroenterology

(Incorporating the American Journal of Gastroenterology)

A monthly journal of Gastroenterology, Proctology and Allied Subjects

Volume 16 MARCH, 1949 Number 3

SYMPOSIUM ON METABOLISM, NUTRITION AND ALLERGY

ALLERGY AS A FACTOR IN GASTROINTESTINAL DISORDERS*†

LOUIS TUFT, M.D.
Philadelphia, Pa.

That allergic reaction can provoke gastrointestinal symptoms is undisputed. To prove that assertion, one need only witness the abdominal pain, nausea, vomiting and even diarrhea which follows almost immediately after the ingestion of a small amount of egg-white by an egg-sensitive child. In such a patient, the gastrointestinal mucosa is an allergic shock organ containing specific allergic antibodies. These react promptly upon direct contact with the egg-white antigen to provoke an allergic reaction, which in turn is responsible for the patient's symptoms. A specific positive reaction to egg-white can be demonstrated by direct skin test and allergic antibodies or reagins can be found in the patient's blood. All this constitutes unquestioned evidence that a specific allergic reaction was responsible for the gastrointestinal symptoms. If this could be duplicated in other patients, the question as to the significance of allergy in gastrointestinal disorders and the problem of gastrointestinal allergy itself would be solved easily. Unfortunately, however, clear-cut allergic gastrointestinal reactions like that to egg-white are the exception rather than the rule. More often the patient presents gastrointestinal symptoms which can be provoked by many causes, both organic and functional. When a definite organic factor cannot be determined, the symptoms then are attributed to functional disturbances including allergy. Conclusions as to the importance of the allergic factor often depends upon evidence which is quite meagre in contrast to the definite evidence obtained in the egg-white sensitive patient. It is difficult therefore to evaluate properly the exact role of allergy in gastrointestinal disorders. It also is practically impossible in view of conflicting reports and statistics to give even an approximate idea of its incidence. Your president's invitation to speak to you, therefore, has given me a welcome opportunity to review this subject at this time and if possible, to summarize the present status of allergy in relation to gastrointestinal disorders.

*Read before the Thirteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 7, 8, 9, 10 June 1948.

†From the Clinic of Allergy and Applied Immunology, Temple University Hospital and Medical School, Philadelphia, Pa.

In the first place, although gastrointestinal symptoms due to allergy usually are intrinsic and result from direct contact with the offending allergen, either food or drug, they also may be extrinsic and be provoked by allergic reactions in other organs. For example, young children with asthma frequently have abdominal pain and vomiting during the course of the asthmatic paroxysm. Likewise, nausea and vomiting are among the cardinal symptoms of migraine, whether due to allergy or to other factors. Seasonal gastrointestinal symptoms occasionally are present in patients with late hay fever. Several of my hay fever patients developed belching or abdominal pain or discomfort only during the hay fever season and never at other times. These symptoms disappeared at the end of the hay fever season but recurred each succeeding one. The reason for the production of such symptoms is not known. But extrinsic allergies are infrequent causes of gastrointestinal symptoms compared with that provoked by direct contact with the offending allergens.

Although both foods and drugs may be excitants, foods definitely are more frequent factors. While food allergens usually provoke gastrointestinal symptoms, they also can cause symptoms in other organs like the skin, the respiratory system, brain, etc. Hence, although gastrointestinal allergy usually is due to food allergy, food allergy need not necessarily produce gastrointestinal symptoms. Probably the most frequent source of error is the tendency to attribute gastrointestinal symptoms following ingestion of foods to food allergy rather than to food intolerance. We frequently are asked, especially in hospital practice, to study patients from an allergic standpoint because they state that they develop such symptoms as belching, nausea, abdominal discomfort, distention or pain after eating certain foods. The mere fact that a food disagrees with a patient is no reason to assume that it is due to a food allergy any more than because a person sneezes means that he has hay fever. Sneezing is a normal reaction of the nasal mucosa and may be provoked by simple chemical or mechanical irritation of the nose in any person. Similarly, gastrointestinal symptoms may be provoked in many individuals by certain foods either because of mechanical irritation or because of altered physiology. This is true, for example of coarse, highly indigestible vegetables like onions, radishes, cucumbers, cabbage, etc. Certain persons can eat these foods, even in large amounts, with impunity. Others develop digestive symptoms not because of allergy but because of physiological alteration in their digestive capacities although they might be able to tolerate these foods in smaller amounts. Even though these foods contain relatively small amounts of active allergen in contrast to a pure protein like egg, they can provoke allergic symptoms like urticaria or asthma in a small proportion of individuals. Such symptoms are definitely abnormal and can be produced by small amounts of the food—hence, they are truly allergic. On the other hand, the gastrointestinal symptoms provoked by such foods commonly occur in allergic or nonallergic individuals alike after eating those foods. They are not pathologic but are the result of altered physiology; hence they should be classified as examples of food intolerance to distinguish them from true food allergy.

It is extremely important, therefore, that the gastroenterologist make this distinction between food allergy and food intolerance. As a rule, it is not difficult, especially in relation to foods which are hard to digest and if the patient has no other allergies. Even then, it still is better to attribute the gastrointestinal symptoms to food intolerance unless proved otherwise. But if these symptoms follow the eating of a readily digested food like milk, differentiation is not always as easy. If milk, even in small amounts, induces nausea or vomiting and there is no organic reason for its development, a milk allergy is possible. But if the ingestion of milk causes belching or diarrhea, it is not always easy to decide whether this is due to allergy or perhaps to some alteration in enzyme content or in the intestinal flora or to similar physiologic reasons. If the patient has other allergic manifestations or has a positive allergy family history and especially if a specific positive skin reaction to milk is obtained, the existence of allergy rather than of intolerance to milk is more likely. Actually, little difficulty in diagnosis is experienced in deciding that allergy to easily digestible foods which contain relatively large amounts of allergenic proteins as for example, eggs, milk, cereals, lean meats, peas, etc. may be responsible for gastrointestinal symptoms. It is only relatively indigestible foods like coarse vegetables containing relatively small amounts of allergen, which offer difficulty since they are more likely to induce reactions of food intolerance.

Another food disagreement which may cause diagnostic difficulty is intolerance to fats or to sugars recently described by Tumen and me[1] and which we have found hard to classify as allergic. Patients with fat intolerance develop such gastric symptoms as flatulence, heartburn or abdominal pain after the ingestion of any kind of fatty or fried foods.

The intolerance exists in relation to all fats (vegetable or animal) and not to any specific one—thus the patient cannot tolerate bacon or chicken fat (yet they can eat ham or chicken); also foods fried in crisco or lard or even butter or oily dressings, fatty fish, etc. They often are regarded as having gallbladder disease because of their difficulty in digesting fats. They sometimes are subjected to cholecystectomy without relief of symptoms and perhaps only on the basis of impaired gallbladder function upon x-ray examination. Exclusion of all fatty foods from the diet and its restriction to foods containing as little fat as possible has been followed by relief of symptoms. This is illustrated in the following case report:

Male, age 37, studied first because of allergic rhinitis and so-called sinus headaches, which responded within a year to allergy treatment. He returned four years later because of frequently recurring migraine headaches, associated with such gastrointestinal symptoms as dyspepsia and diarrhea. He stated that he had been subject to these symptoms for many years and has been studied for it by a gastroenterologist but no organic disease was found. A tentative diagnosis of cholecystitis was made, duodenal drainage given and a low-fat diet advised.

As part of the allergy study, the patient was put on an allergy trial diet which was low in fat. His headaches became less frequent, the gastrointestinal symptoms diminished greatly, he became free of indigestion and diarrhea disappeared. The

patient recalled that he never was able to tolerate fatty foods or fats in general but had attributed this to his "gallbladder" condition. When he tried eating fats, even that in eggs, the symptoms recurred. Since avoiding fats, he has had little or no gastrointestinal symptoms. He was able to take sugars without difficulty.

This patient represents an example of many others who have symptoms of fat intolerance and who get relief from avoidance of fats. Patients with intolerance to sugars on the other hand tend to complain of diarrhea and flatulence (both gastric and intestinal) as in the following patient:

Female. Age 42. This patient has had recurrent attacks of diarrhea and abdominal cramps for about 15 years. Repeated intensive studies never revealed organic disease of the bowel. Because of the presence of nervous tension, a diagnosis of irritable colon of neurogenic origin was made. The patient came from a family of which various members suffered allergic disturbances. She herself developed hives after taking chocolate and fish and also had had mild angioneurotic edema of unknown origin. She suspected that the ingestion of certain foods—fish, chocolate, excessive coffee and orange caused diarrhea.

Incomplete skin tests showed sensitivity to chocolate, tomato and spinach. On elimination trial diets, improvement followed but subsequent additions were not continued long enough to determine definitely those foods which were not tolerated. It was found, however, that the ingestion of fats and sugars frequently provoked flatulence and diarrhea and that reducing their intake often brought an improvement. One event may be described as illustrating the effect of sugar ingestion. While on vacation and at a time when no food has been taken for a number of hours, the patient ate some pure maple-sugar candy. Within one-half hour violent diarrhea occurred. The patient recalled similar episodes and since then has observed that any type of concentrated sweets frequently has a laxative effect, inducing watery bowel movements.

The symptoms presented by both these patients could be duplicated by many others with gastric or intestinal symptoms or both, apparently provoked by fat or sugar intolerance. In such patients marked relief follows elimination of these substances from the diet or their reduction to small quantities. The intolerance seems to be general and is not restricted to single fats or sugars. In patients who are sugar-sensitive, any sugar (e.g. cane, malt, or dextrose) produces diarrhea and symptoms even follow the intake of large amounts of starchy food. Fat intolerance also is manifested indiscriminately toward all fats such as butter, vegetable oils, egg yolk and the minimal fats taken with fat meats. Difficulty in digestion of the latter class of fats explains why patients could eat large amounts of lean meats such as ham or beef if this is boiled or baked but could not eat the same meats if fried or prepared with the fat retained. The same patient might tolerate white meat of stewed or roast chicken but may have distress after eating fried chicken or even the dark meat of the fowl.

While many of the patients which we have seen with fat and sugar intolerance were allergic, having been referred usually for allergy study, this form of intolerance

also can be found in other individuals who do not suffer with allergy. The large number of patients who claim not to tolerate fatty and fried foods—and who are often erroneously considered to have gallbladder disease—probably includes many who have the form of fat intolerance just described.

Certain aspects of the intolerance to fats and sugars argue against this being due to allergy—as this term is generally defined. Firstly, no patient was encountered who was intolerant to only one specific fat or sugar. The intolerance seems to be directed against entire classes of these substances so that it was impossible, for example, to substitute vegetable fats for butter or dextrose for sucrose. Furthermore, the patients usually were able to eat the protein portions of meat or chicken or egg but could not digest these proteins if they were not separated from the fats naturally associated with them. Since specific allergic reactions usually involve only proteins, one must seek some other reason for these adverse reactions to nonprotein substances. It is possible of course that the allergy may exist to one of the split products (e.g., aldehydes in the case of fats) but such an explanation awaits confirmation.

There is at present no satisfactory explanation for the intolerance to fats and sugars observed in these and other patients. The digestion and absorption of fats is a relatively complicated process. It depends upon the presence in the bowel of adequate quantities of bile acids and of pancreatic and intestinal enzymes, and upon the ability of the intestinal mucosa to absorb the fatty acids and glycerol which are the end products of fat digestion. The digestion of sugars is a much simpler process—consisting largely of conversion of polysaccharides to monosaccharides and the absorption of these. It may be that patients who suffer with fat and/or sugar intolerance have some defect in their ability to absorb these substances. But, regardless of the reason, fat and sugar intolerance can be important causes of gastrointestinal symptoms in allergic or nonallergic individuals alike.

Now I would like to say something about the relationship of allergy to specific gastrointestinal disorders. Time will not permit discussion of all of these, so I will limit it to peptic ulcer, the "irritable" colon and to chronic nonspecific ulcerative colitis.

The *relationship of food allergy to peptic ulcer* long has attracted attention. The experimental production of acute gastric ulcers in the anaphylactically-sensitized animal suggested that allergy might be the basis of peptic ulcer. Likewise, as indicated by several writers, if food allergy can produce a canker sore in the mouth, it ought conceivably to be able to produce a similar lesion in the gastric or duodenal mucosa. But despite these theories, definite proof of an allergic basis for chronic ulcers in the human being has been difficult to obtain and has been the subject of considerable controversy. Most of the evidence offered to support this theory depends upon the demonstrations of specific food allergy, often by diet trial. Removal of the offending food from the diet was followed by relief of the ulcer symptoms whereas reintroduction into the diet caused their reappearance. Many of the reported cases in which this was manifested were individuals with typical ulcer symptoms but no demonstrable lesion (viz. by roentgen ray). This

relationship was not quite so clear in patients in whom a definite ulcer was found —thus Kern and Stewart[2] found evidence of the relationship of allergy to ulcer in a small but appreciable number of patients. Ehrenfeld and his coworkers[3], on the other hand, from a study of a group of patients with peptic ulcers and a similar control group of allergy patients found no difference in the incidence of allergy in the ulcer group or of ulcer in the control group from that which is found among the general population. They conclude therefore at least upon the basis of their evidence that there is no valid reason to assume that allergy plays a significant role in the etiology or pathogenesis of peptic ulcer. But despite these differences, all writers agree that food allergy can provoke symptoms which may simulate peptic ulcer and should be differentiated especially in those with no demonstrable lesions. This is exemplified in the following case report:

Male. Age 27. Referred because of repeated attacks of allergic rhinitis, migraine headaches and occasional urticaria. For many years, patient had attacks of heartburn and epigastric pain occurring 2 to 3 hours after meals and relieved by ingestion of soda. He showed numerous positive skin test reactions to such inhalants as house dust, feathers and ragweed pollen and to various foods, including especially, milk, wheat and fish. Elimination of the offending foods from the diet was followed within a short time by marked improvement in the gastrointestinal symptoms with complete disappearance of pain and heartburn and lessening of feeling of fatigue and of headache. This improvement has persisted now for more than 15 years. Gastrointestinal symptoms appear now only after dietary indiscretion—thus they are noted especially after the use of milk even in smallest amounts like in butter; also after eating wheat or fish.

This case report illustrates symptoms resembling peptic ulcer which disappeared upon the elimination of foods, especially milk and wheat to which the patient was allergic. This is important also in ulcer management for if the patient is allergic to milk and is on a Sippy regime, he will not respond to treatment unless the offending food is eliminated. Food allergy therefore may be significant in this sense in the treatment of peptic ulcer. But whether or not allergy is the basis of peptic ulcer or in what proportion it may cause it, still remains an unsettled question with most of the evidence at present against it.

Turning now to the *irritable colon* or *mucous colitis*, there has been considerable evidence to show that allergy may be a factor in its causation. Thus it has many similarities to bronchial asthma which also is characterized by spasm and the production of excessive mucus; furthermore, specific reactions to certain foods as causes of the colonic condition have been found sufficiently often to make the relationship of allergy more certain. In my own experience, milk and wheat are prominent offenders. But despite this evidence, many gastroenterologists and other practitioners have been so imbued with the thought of a psychosomatic background that all other factors including food allergy are disregarded. Take for example the following case:—

A 28 year old white male physician, first seen while a medical student, because of perennial allergic rhinitis and asthma. Intracutaneous testing revealed significant

positive reactions to house dust, corn, wheat, almond, asparagus, celery, shad, shrimp and to timothy, plantain and ragweed pollens. On a regime of elimination of test-positive allergens and appropriate desensitization, he was symptom free until army maneuvers in the Carolinas. He developed nasal symptoms from sleeping on pine needles and severe diarrhea from ingestion of corn meal. The nasal symptoms disappeared when away from pine contact and the diarrhea cleared up on elimination of test-positive foods. After the ingestion of ice-cream, the diarrhea reappeared. Subsequent investigation revealed that the ice-cream was prepared with a great deal of cornstarch. He was warned to avoid this substance and became symptom free. Two dietary indiscretions in which cornstarch was ingested resulted in diarrhea. Avoidance of cornstarch as well as of the other positive foods produced a complete remission in gastrointestinal symptoms. It is an interesting sidelight in this case that when the patient was being investigated by army authorities to determine whether he should be discharged for physical disability, he was placed on a full diet because the intestinal condition was considered mostly psychoneurotic. Profuse diarrhea and marked weight loss, necessitating prompt hospitalization, followed. The patient was then placed on an allergy diet and when sufficiently improved was given a discharge because of physical disability.

While psychosomatic factors undoubtedly are important in causing irritable colon, other causes should not be ignored. As in asthma, the removal of the basic allergy factors sometimes will make the patient less susceptible to exacerbations produced by emotional upset.

These considerations apply also in relation to the last condition I wish to consider, namely, *chronic nonspecific ulcerative colitis*, in which similar attempts also have been made to incriminate food allergy as a cause. Andresen[4] is the outstanding proponent of the idea that food allergy is responsible for the symptoms in the majority of such patients. He offers as proof the relief obtained by the elimination from the diet of offending foods ascertained by diet trial. Milk seemed to be the most prominent offender with wheat, tomatos, oranges, potatos and eggs next in order of frequency. Rowe[5] also confirmed these findings upon the basis of clinical evidence obtained by the use of his milk-free, cereal-free and fruit-free diets. But other observers, notably Bargen[6] have not substantiated these findings. They believe that most instances are infectious in origin and that allergy is important in only a small number (perhaps 10 per cent) of patients. As with peptic ulcer either food allergy or emotional upsets or vitamin deficiency conceivably could cause aggravation of symptoms. It should be watched for and eliminated whenever found. But until more definite evidence of a specific etiologic relationship is obtained, it would seem unwise to subject all patients with ulcerative colitis to complete allergy studies, unless the history of the patient clearly points to a possible allergic factor.

We have not had the opportunity to study as many of these patients as others but of those studied only one showed definite evidence of allergy. This was a girl aged 10 with ulcerative colitis of 13 months duration for which an ileostomy had been performed a month later. The mother stated that the patient had difficulty

taking egg ever since infancy but except for some sneezing with temperature change, there were no other allergy symptoms. The father had migraine and developed hives upon eating tomatos or rhubarb. Intracutaneous skin tests showed definite positive reactions to eggs, milk, green peas and other foods. To check their specificity, the patient's blood was studied by passive transfer. Specific allergic antibodies or reagins to the following foods were demonstrated:—milk, egg, green pea, spinach, tomato, banana, orange, strawberry and black pepper. Repeated blood counts showed an eosinophilia of from 10 to 16 per cent. The patient was placed on a diet excluding the offending foods. However, it was difficult to determine whether this was beneficial because the patient received biotherapy (streptomycin) at the same time and prior to a colectomy, from which she is now recuperating.

One would not question that this patient has definite evidence of food allergy according to the history, which is verified both by skin test findings and by the finding of specific allergic antibodies in the blood. Yet it still is not possible to say whether we are dealing here with an ulcerative colitis that happened by mere coincidence to affect a patient with food allergy or whether the food allergy was actually responsible for the condition. This is more difficult to prove because the condition was so well established when we first saw the patient. One could not expect that removal of the offending foods would cure this condition anymore than removal of allergens cures a patient with well-established emphysema secondary to bronchial asthma. One can only say, therefore, that allergy may be a factor in certain patients with ulcerative colitis and should be taken care of when present. But whether it is the primary cause or even a frequent one remains to be proved.

Before concluding, I would like to say a word about allergy diagnosis in these conditions. I have purposely avoided the mention of skin tests because their value has been the subject of so much false interpretation. Time does not permit detailed discussion of this phase of the subject. But undoubtedly sole reliance upon the results of skin tests has been responsible for most of the confusion regarding the role of allergy in gastrointestinal disease. Allergy skin tests properly carried out and properly interpreted by those experienced in their use can be valuable adjuncts in diagnosis. But if improperly performed or interpreted, they may give a lot of useless and misleading information which has resulted in pleas for their abandonment at least as a means of diagnosis of food allergy. It is an established fact that gastrointestinal symptoms due to food allergy may exist in a patient who gives negative skin tests. Under those circumstances the determination of the offending food must depend upon proper clinical trial, especially the use of allergy trial diets. While diet trial may seem simple, it too requires considerable skill and judgment for its execution. If improperly used, an important food allergen may be overlooked and prevent the clearing up of the patient's symptoms. I have seen many patients who have been subjected to trial diets in whom the method failed to reveal the offender because of improper application.

In conclusion, therefore, if a patient presents certain gastrointestinal symptoms apparently of functional origin, it first is important to make sure that one is not

dealing with food intolerance rather than food allergy. If this can be done, then proper application of the diagnostic methods including history, skin tests and diet trial will succeed in determining whether or not the condition is upon an allergic basis and also the offending allergen. These procedures will serve to show more definitely not only that allergy may be an important factor in gastrointestinal diseases but they also will dispel much of the confusion as to its reported incidence and its reputed relationship to certain of these diseases.

REFERENCES

1. Tuft, L. and Tumen, H. S.: Fat and Sugar Intolerance as a Cause of Gastrointestinal Symptoms. J.A.M.A. **130**:624, 1946.
2. Kern, R.A. and Stewart, S. G.: Allergy in Duodenal Ulcer. J. Allergy. **3**:51, 1931.
3. Ehrenfeld, J., Brown, A. and Sturtevant, M.: Studies in Gastrointestinal Allergy—Allergy in the Pathogenesis of Peptic Ulcer. J. Allergy. **10**:342, 1939.
4. Andresen, A. F. R.: Ulcerative Colitis:—an Allergic Phenomenon. Am. J. Digest. Dis. & Nutrition. **9**:91, 1942.
5. Rowe, A. H.: Chronic Ulcerative Colitis—Allergy in its Etiology. Ann. Int. Med. **17**:83, 1942.
6. Bargen, J. A.: Medical Management of Ulcerative Colitis. J.A.M.A. **126**:1009, 1944.

AMINO ACIDS IN THE PRODUCTION OF PLASMA PROTEIN AND NITROGEN BALANCE*†

S. C. MADDEN, M.D.
Atlanta, Ga.

Threonine, valine, leucine, isoleucine, tryptophane, lysine, phenylalanine and methionine are the only amino acids required for nitrogen balance in man. An imbalance develops by removal of one of these from the nitrogen intake. There is some evidence that a small supplement of histidine intake is required for human nitrogen balance. Arginine deficiency as a factor in the production of testicular atrophy of male adults needs further confirmation. The remaining amino acid constituents of body proteins can be formed in the body. However, limited dietary intake, particularly in disease, is not to be carried out because the so-called nonessential amino acids may be critically needed for the patient's welfare. The demand may exceed the maximum capacity for synthesis of a nonessential amino acid.

Injection of human plasma and feeding or injection of purified serum albumin as well as the intake of the essential amino acid or acids will produce plasma protein in man to re-establish nitrogen balance where an imbalance exists. Determinations as outlined by Brand and his associates will make known the composition of the human serum albumin examined. The findings may indicate the requirements for the plasma protein formation. Studies for the quantitative amino acid requirements for man are now in process but the results to date are inconclusive. There is, however, evidence that the growing human has a greater requirement than the adult. This is exemplified by the need of at least 15 times as much tryptophane for infants as for adults.

Production of plasma protein and nitrogen balance via parenteral administration of amino acids can be much over-used and abused. Oral feeding skillfully applied may be more advantageous, in some instances, than inept and inadequate intravenously given nitrogenous solutions. Nevertheless, early and appropriate intravenous use of the currently available solutions are probably more helpful in most cases.

Synthetic mixtures consisting mainly of natural amino acids and low in glutamic and aspartic acids may permit more rapid infusion without resultant nausea and vomiting. These mixtures may further stimulate the use of parenteral feedings for those patients requiring rest for the gastrointestinal tract. It seems that nitrogen balance in humans is greater with oral than intravenous feeding of the same amino acid mixtures.

Pertinent findings relative to amino acid feedings are as follows:

1—Amino acid excretion in the urine is greater after intravenous infusions than after oral feeding.

---

*Abstract of a paper read before the Thirteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 7, 8, 9, 10 June 1948.
†Abstracted by A. X. Rossien, M.D.

2—There is less excretion of amino acids with feeding of natural protein than with the ingestion of amino acids.

3—Feeding of incomplete proteins or incomplete amino acids mixtures yields higher excretions of amino acids.

4—Wherever practical, oral feeding is preferable.

5—Intravenous infusions of peptides are less metabolised than are amino acids.

6—Tissue cells prefer amino acids over peptides.

ENDOCRINE DISTURBANCES IN GASTROINTESTINAL CONDITIONS

MORTON S. BISKIND, M.D.
New York, N. Y.

Affections of the gastrointestinal tract, as is well known, may impair the nutritional status. Any factor which operates to limit intake, or to impair absorption or utilization of essential nutrients, or to increase the requirement for these substances, or to enhance their rate of destruction or excretion, will cause nutritional deficiency. Various functional disturbances which lead to protracted spasm of the gastrointestinal musculature, or to chronic diarrhea (or both), peptic ulcer, affections of the liver, gallbladder and bile passages, amebiasis and other chronic infections of the colon, allergic reactions, restricted diets and adsorbing agents, certain of the sedatives, sulfa drugs, penicillin, arsenic compounds and quinoline derivatives used in the treatment of the conditions mentioned, all act to diminish the tissue levels of the different vitamins. Deterioration of the nutritional status, in turn, leads to further disturbances in the gastrointestinal tract, involving aberrations of motility and changes in the mucosa, and further diminishing the ability to absorb essential substances.

As a result of any one or any group of these factors, various secondary disturbances occur. Among these are a number of endocrine dyscrasias related to nutritional impairment of hepatic function.

Twenty-two years ago, soon after the first crude preparations of estrogen became available, H. M. Evans and Burr made the initial observation on which the studies to be described here were based. They noted that their preparations of estrogen were less effective when injected intraperitoneally than when given subcutaneously. The explanation for this curious fact was not forthcoming until 8 years later, when Zondek demonstrated that liver inactivated estrogen *in vitro*.

In 1938, G. R. Biskind devised an ingenious technic for studying this problem *in vivo*. Pellets of crystalline estrogens or androgens were implanted into the spleens of castrate female or male rats. The vessels of the spleen drain into the portal circulation and the absorbed steroid must therefore pass through the liver before reaching the systemic circulation. Thus, a castrate female with a pellet of estrone or estradiol in the spleen, remains anestrous; but if the spleen containing the pellet is transplanted subcutaneously, and after development of a collateral circulation, the pedicle is ligated, the animal goes into continuous estrus. Analogous results may be obtained in the male, using the weight of prostate and seminal vesicles as the indicator. The livers of both male and female rats were found to inactivate both estrogens and androgens.

Owing to experimental and clinical studies indicating that morphologic changes in the liver may result from deficiency of factors of the Vitamin B-complex, the

*Read before the Thirteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 7, 8, 9, 10 June 1948.

aforementioned technic was applied in 1941 by the author and G. R. Biskind to the problem of nutritional impairment of hepatic function. Castrate female rats with pellets of estrone in their spleens remained anestrous so long as they were maintained on a complete diet. But when they were placed on a Vitamin B-complex-free diet, they became estrous and remained so. Addition of the B vitamins promptly restored the anestrous state and subsequent depletion again led to estrus. Thus the flow of estrogen through the liver could be controlled at will, by withholding the B vitamins or restoring them to the diet. Similar effects were obtained with animals having one ovary transplanted to the spleen and the other removed. Using both *in vivo* and *in vitro* technics with crystalline steroids, numerous other investigators have confirmed and extended these original findings. However, there appears to be no necessary correlation between the functional disturbance and morphologic changes. Failure of inactivation of estrogen occurs in livers that are normal histologically, while livers seriously damaged histologically *may* continue to inactivate estrogen.

Subsequently we investigated the inactivation of androgen in the liver. In this case a different result was obtained, for there was no significant impairment of this function during Vitamin B-complex deficiency. Estrogen ceases to be inactivated in the liver while androgen continues to be destroyed; thus a serious alteration in the estrogen-androgen equilibrium must result in deficiency of the Vitamin B factors.

These findings suggested certain possible clinical applications, and led us logically to a series of observations in the human being, which, it soon became apparent, required an unorthodox approach to therapy.

The investigations already described which indicated an alteration of the estrogen-androgen equilibrium in deficiency of the Vitamin B-complex, led us to investigate whether there was any correlation between nutritional deficiency and the occurrence of syndromes related to excess estrogen. In the female these are meno-metrorrhagia, cystic mastitis, premenstrual tension, hyperestrogenic forms of amenorrhea or oligomenorrhea, certain types of excess libido, certain types of dysmenorrhea, sterility due to persistence of an estrogenic endometrium, neoplasms of the breast and uterus, postpartum subinvolution of the uterus, and endocrine obesity characterized by excess deposits of flabby adipose tissue over hips, thighs and abdomen; in the male, testicular atrophy, gynecomastia, diminished libido and potency and infertility (and, occasionally, endocrine obesity of the type just described). Such a correlation was indeed found to exist. Patients with these syndromes had various indications of nutritional deficiency and the endocrine disturbances responded promptly and often dramatically to intensive, complete nutritional therapy. Atrophic glossitis, gingivitis and cheilosis were common; other visible lesions were the characteristic seborrheic ("muddy") complexion, a seborrheic, erythematous eruption about the alae nasae, keratosis toward the inner canthus of the lower eyelids, injection of the conjunctivae, especially about the periphery of the corneae, splitting of the fingernails in layers, palmar erythema, cutaneous vascular "spiders" and occasionally actual pellagrous dermatitis, in-

volving the malar areas of the face in the typical "butterfly" distribution, or the ears, hands, wrists, elbows, ankles or knees, being almost always symmetrical and bilateral. Associated with the objective disturbances there are usually changes in the nervous system; excessive nervous irritability, emotional instability, insomnia, headaches, impairment of memory for recent events, "clouding" of consciousness, excessive fatigability, "restless legs" and peripheral neuritis, manifested in the early stages, by diminished vibratory sense, and by spontaneous cramping of the muscles, especially the gastrocnemi, and later by pain in arms and legs and lumbar area, loss of abdominal, achilles and patellar reflexes, and eventually actual muscle weakness.

In the course of the seven years that these studies have been carried on, more than 900 cases involving pathologic uterine bleeding and the like, were observed and treated with Vitamin B-complex in three independent series of cases in eastern, western and mid-western portions of the United States (in collaboration with Drs. G. R. and L. H. Biskind). The results were uniformly favorable, for not only did the endocrine disturbances clear up but the indications of nutritional deficiency subsided simultaneously and vast improvement in general health was the rule. These clinical results have been confirmed by several widely separated groups of workers in the United States and other countries. In another series, administration of Vitamin B-complex during pregnancy led to striking reduction in the incidence of postpartum subinvolution of the uterus and its complications.

The association of lesions of nutritional deficiency with aberrations of the sexual function in the male was found to be no less common than in the female. In studies on more than 200 males, infertility, (with definite impairment of number and morphology of spermia), testicular atrophy, gynecomastia, and impaired libido and potency, were found frequently associated with lesions already described, and with hepatomegaly. In our experience, striking improvement in all these conditions has occurred with adequate nutritional therapy. Improvement in the sperm counts and in morphology, with subsequent proved fertility, recovery of normal libido and potency, improvement in size and texture of the testicles and subsidence of gynecomastia, have all occurred with vitamin therapy; the nutritional lesions and hepatomegaly subsided simultaneously.

Still another endocrine disturbance related to impairment of hepatic function and often associated with sex-endocrine disorders of the types described, is diabetes. It has long been customary to think of diabetes solely in terms of insulin deficiency, simply because insulin, in most caes, improves carbohydrate metabolism. But during a decade of fundamental investigations, Soskin and his collaborators have shown that, provided the barest minimum amount of insulin is present in the body, it is the liver and not the pancreas that controls the blood sugar, Thus:

(1) In pancreatectomized animals receiving a constant intravenous injection of insulin just sufficient to maintain normal blood sugar, administration of dextrose yields *normal* dextrose tolerance curves.

(2) In hepatectomized animals with intact pancreas, receiving a constant intravenous injection of dextrose just sufficient to maintain normal blood sugar, administration of additional dextrose yields *diabetic* dextrose tolerance curves.

(3) When the liver is damaged by a toxic agent, the *diabetic* type of dextrose tolerance curve is obtained.

Observations indicating the occurrence of lesions in diabetes now known to be nutritional in origin, were recorded in the medical literature 40 years ago. Stockton, in 1908, wrote, "The tongue in diabetes is large, red, beefy, and bordered with a fissured margin . . . . " a classical description of pellagrous glossitis. Futcher, a year earlier, reported functional changes in the nervous system of diabetics, now known to be nutritional in origin. Many other neglected observations during the past half-century pointed to a nutritional defect in diabetes.

In approximately 150 diabetics that we have observed over a period of 5 years (of which 94 have previously been reported), avitaminotic disorders were found to be almost invariable. And a high incidence of associated sex-endocrine disturbances of the types described was noted in these patients. Nutritional therapy not only affected the avitaminotic defects, but in numerous patients dramatic reductions in blood sugar occurred on vitamin therapy alone, in others the insulin requirement could be reduced or eliminated. The related endocrine disturbances subsided simultaneously and even in the groups of patients in whom it was not possible to reduce the insulin requirement there was invariable improvement in general health.

Thus, diabetes appears in large part, not to represent insulin deficiency, but impaired hepatic response to endogenous insulin, which need not be deficient. The response of the liver to insulin, whether endogenous or exogenous, can often be greatly enhanced by nutritional therapy.

I am sure it is no secret to most of you that this concept of a nutritional approach to certain endocrine problems, despite extensive supporting evidence which goes back more than half a century, has been received with skepticism, disbelief and even open hostility. This is not surprising since it involves simultaneous and extensive reorientation in two fields of medicine: Recognition of lesions of avitaminosis, now often overlooked; a revision of the general attitude toward the adequacy of the usual dietary intake of vitamins; a new understanding of the basic principles of nutritional therapy; and finally, application of these new ideas to endocrinology, in which long tradition dictates an entirely different approach. Changes of this kind are never made easily or rapidly. In fact, we must confess to a considerable initial skepticism ourselves; this was only gradually dispelled by the compelling nature of the accumulating evidence.

The Method of Nutritional Therapy

For adequate nutritional therapy three basic requirements must be fulfilled: (1) Complete therapy; (2) Intensive dosage by routes assuring adequate utilization; (3) Persistent administration. Many failures result from disregard of one or more of these principles.

Because the use of single drugs has a strong tradition in modern medicine (in reaction to the unscientific polypharmaceutic therapy that persisted to two or three generations ago), it is common practice to administer thiamine or niacinamide or riboflavin or ascorbic acid alone in large doses in an effort to counteract an apparently predominant deficiency of one of these factors. But single deficiencies are impossible in clinical medicine. Since the water soluble vitamins occur together, an inadequate diet is certain to be deficient in many factors simultaneously. And even in an otherwise adequate diet subjected to cooking, processing of other types, storage, etc., factors which lead to loss of thiamine from the diet, for instance, inevitably lead to loss of other substances that occur with it and have similar solubilities, or are also labile to heat, alkalinity or oxidation. Similarly, factors which impair absorption, increase the requirement, increase excretion or interfere with utilization (e.g., excess physical activity; alcoholism; various drugs such as sulfonamides, penicillin, estrogens and thyroid; various toxic materials used in industry; gastrointestinal disorders, biliary or liver disease, and the like) which operate to produce nutritional deficiency even on an optimum diet, tend inevitably to produce deficiencies of several factors at once. Lack of adequate protein, common in deficient diets, tends to disturb cellular enzyme systems, which also leads to loss of many factors at once.

Not only are deficiencies multiple, but administration of single vitamins (or even of a combination of a few of them) not only is usually ineffective but may actually lead to serious disturbance of a tenuous nutritional equilibrium and production of new deficiency lesions. In the early use of niacin in the treatment of pellagra the enthusiastic preliminary reports of rapid healing of the dermatitis and the glossitis were soon followed by pessimistic accounts of the appearance of secondary lesions, such as cheilosis and peripheral neuritis. It was then found that addition of an adequate natural source of nutritional factors to the therapeutic regime led to subsidence of all the lesions. Similarly, in a recent study by Hibbs on treatment of beri-beri in prisoners of war, administration of thiamine alone failed to affect the neuritis, although there was definite amelioration of this condition in patients who received the whole B-complex.

Thus, it is essential to recognize that substances not yet isolated or identified, are present in natural sources (especially in liver) and that these unidentified factors are quite as important to nutrition as those already available in pure form.

Depending on the original nutritional status and response of the patient, adequate nutritional therapy might require 2 or 3 capsules or tablets a day of a preparation, which provides intensive dosage of the crystalline water-soluble factors and Vitamins A, D, and E (e.g., per dose, Vitamin A 10,000 units, Vitamin D 500 to 1,000 units, alphatocopherol 10 mg., thiamine 10 mg., riboflavin 5 mg., pyridoxine 1 mg., pantothenic acid 5 mg., niacinamide 50 mg., and ascorbic acid 100 mg.). In addition, a Vitamin B-complex preparation containing a natural source or sources, preferably liver, is essential. This must be given in a dosage

sufficient to provide material derived from at least 45 gm. and occasionally as much as 150 gm. of the fresh natural source a day.

For this purpose two types of Vitamin B-complex preparations are especially valuable: (1) nutritional extracts of liver fortified with crystalline B vitamins—these preparations contain the total aqueous, or 80 per cent alcohol-insoluble fraction of liver, or a combination of the two (lipoid factors of liver, which also comprise essential nutritional elements, may be included) and are given in dosages representing from 80 to 120 gm. of fresh liver a day (usually 9 to 12 capsules or equivalent amount of liquid); and (2) desiccated whole liver, either fortified with B vitamins or unfortified—usually at least 9 gm. (eighteen 0.5 gm. capsules or tablets) is given daily, sometimes more. The minimal dose provides the equivalent of 45 gm. fresh whole liver a day.

Desiccated liver, being unfractionated, provides probably the best available source of the as yet unidentified factors essential to nutrition, but it must be given in relatively large dosages to be effective; these dosages are, however, quite feasible. All the products are given in divided doses after meals. It is important of course to make certain that the diet contains adequate protein, since in its absence the B vitamins cannot adequately be utilized.

A number of severely deficient patients (and this is especially true of those with gastrointestinal disorders) require parenteral therapy in addition, with a frequency varying from daily to three times a week. This usually provides, in each injection, thiamine 10 to 60 mg., riboflavin 5 to 10 mg., pyridoxine 5 to 20 mg., calcium pantothenate 5 to 50 mg., and niacinamide 50 to 250 mg. Sodium ascorbate 50 to 100 mg., may be mixed with the B vitamins in the same syringe. Injections should be given *slowly* intramuscularly, either intragluteally or deep in the outer aspect of the thigh. Parenteral liver extracts, which are purified mainly with a view to increasing the antianemic potency, are not satisfactory for nutritional therapy in dosages feasible to inject; even the so-called "crude" preparations contain only insignificant amounts of the B factors. Even after all avitaminotic lesions have healed and the secondary disturbances are under control, it is necessary to maintain the patients indefinitely thereafter on at least 5 to 10 times the maintenance amounts for persons who have never been deficient, often much more.

For those interested in references to the original literature, these may be found in Vitamins & Hormones **4**:147-185, 1946, American Journal of Clinical Pathology **16**:737-745, 1946, and Journal of Gerontology **2**:303-314, 1947.

These investigations have been aided by grants from U. S. Vitamin Corporation, Lederle Laboratories Division of American Cyanamid Company and Rawl Chemical Company, all of New York.

NUTRITIONAL THERAPY: SOME FACTS AND PROBLEMS*

HERBERT T. KELLY, M.D., F.A.C.P.†
Philadelphia, Pa.

The biochemical and physiological process of nutrition is influenced adversely by disease and surgery. However, like all medical procedures, nutritional therapy should be undertaken only after current tissue status has been evaluated quantitatively and qualitatively and resultant recommendations prove psychosomatically acceptable to the individual.

In health and in disease, body nutrition is in a state of flux. Kruse[1] has shown that for the biologically active form of a nutrient, nutritive balance depends on the relationship of tissue supply to tissue requirement. This ratio, $\frac{\text{supply}}{\text{requirement}}$, is constantly altered by a variety of external and internal forces acting on either or both members of the proportion (Table I). The conditions include socio-economic, physical, chemical, dietary and psychosomatic factors, a series of positive forces which are capable of producing a negative nutritional balance. The number and type of conditions altering the ratio at any one time are usually multiple and their degree of influence relative. Those conditions which increase supply or decrease requirement, generally have a favorable effect on tissue nutrition; those acting in the opposite direction, an unfavorable consequence. Hence, in intestinal obstruction, for example, the transport of nutrients is impeded, thereby decreasing supply to the tissues. Unless suitable replacement therapy is instituted, a severe nutritional deficiency is incurred. Acting on the other member of the ratio, liver disease increases tissue requirement for protein. Unless this is supplied in adequate amounts, a deficiency state results or is aggravated by an already existing deficiency. Of the two types of nutritional deficiency, the chronic state is more prevalent. It is persistent as opposed to the acute deficiency which either disappears or leads to death. Both are characterized by velocity, intensity and duration. However, in the chronic type, a long period of time is necessary for tissue pathology to become evident.

This integrated concept demonstrates the multiplicity and relativity of conditions influencing body nutrition. It may indicate that reliance on present physical examination and laboratory methods is no longer feasible. Absence of tissue changes is not indicative of adequate nutritional status. An evaluation of nutrients in the blood stream reflects only current tissue status as determined by recent diet. Therefore, short-term dietary data, as elicited by most physicians, is only of limited value. A final comment on diagnostic standards concerns signs and symptoms, particularly those on the gastrointestinal and psychological levels. Although not diagnostic criteria in themselves, they may be associated with nutritional deficiency or on the other hand may be referable to psychoneurosis.

*Read before the Thirteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 7, 8, 9, 10 June 1948.
†Associate in Medicine, Graduate School of Medicine, University of Pennsylvania.

The diagnostic and therapeutic implications of Kruse's total point of view are clearly applicable in all fields of medicine. Two of the conditioning criteria, food habits and psychosomatic relationships, often regarded somewhat nebulously by the clinician, have particular significance in optimal nutritional management of the patient.

TABLE I

CLASSIFICATION OF CONDITIONS INFLUENCING NUTRITIVE BALANCE[1]

External Environment

A. *Socio-Economic*
- Living conditions
- Working conditions
- Available foods
- Ability to seek food
- Income
- Education

B. *Physical and Chemical*
- Radiant energy
  - Light, infra-red
  - Ultra-violet, x-ray
  - Radioactive
- Temperature
- Mechanical
  - Trauma
  - Physical movement
  - Pressure; irritation; friction
  - Occlusion
  - Dentures
- Toxicants

C. *Dietary*
- Form of nutrient
  - Provitamin: analogue
  - Potential or intrinsic biological activity
- Level
- Imbalance-Disproportion
- Interrelations
  - Protein-Carbohydrate-Fat
  - Vitamin-Vitamin
  - Vitamin-Protein
  - Vitamin-Carbohydrate
  - Vitamin-Fat
- Inhibitors-Antagonists
  - Anti-vitamins
- Enzymatic destruction
- Autoxidation-rancidity
  - Oxidants-autoxidants
- Processing of foods
- Availablity of nutrients
  - Precipitation
    - Phytic acid-Iron
    - Oxalic Acid-Calcium

Bodily Environment

A. *Digestive and Metabolic Channels*
- Functional form of nutrient
- Ingestion
- Digestion
- Absorption
- Transport
- Formation of enzyme
- Breakdown of enzyme
- Metabolism
  - Elaboration
  - Utilization
- Storage
- Metabolic level
- Excretion
- Biosynthesis
  - Intestinal synthesis
- Biodegredation
  - Intestinal destruction

B. *Functions and Reactions*
- Disease
  - Degenerative
  - Neoplastic
  - Organic
  - Toxic
  - Infectious
- Chemotherapy
- Endocrine relationship
- Nutritional status
  - Morphology and physiology of tissue
- Growth
- Pregnancy and Lactation
- Work
- Psychobiology
  - Food Habits
    - Hunger and Appetite
    - Psychosomatic Reactions

"Food habits" is an inclusive term, encompassing the reasons why the individual selects and consumes certain portions of the available food supply. They are determined in part by external pressures, and in part by basic bodily constitution, and biochemical, physiological and psychological influences acting directly or indirectly within the individual (Table II). Eating practices are based on more than socio-economic factors, although these, of course, are often major determining factors. Fundamentally, food habits depend on appetite and hunger. Ivy[2] has defined hunger as a bodily state characterized by an inherent, instinctive drive

for food of any kind. Appetite, on the other hand, is a conscious phenomenon, due largely to mental and emotional associations, which causes an individual to like specific foods. Physiologically it is mediated through the stimulation of the sense organs—sight, temperature, odor, texture and taste of food. Strictly speaking, the inclusion of the latter may now be somewhat out-dated, since Schneider's work[3] indicates that taste is not an entity in itself, but a synthetic sense, composed of touch and a trophic quality related to vibration. Via this sensitizing trophism, the papillae of the tongue react to sweet, salt, sour and bitter qualities. The odor of food is also a significant determinant of appetite. Before meals there is an increased olfactory acuity, although this does not occur when food has been ingested between meals. Postcibally, upon satiation, acuity is decreased[4]. During

TABLE II

FACTORS DETERMINING FOOD HABITS

External Environmental Influences

1. Living conditions
2. Working conditions
3. Income
4. Education
5. Social strata
6. Available foods
   a. agriculture
   b. technology-food processing
   c. food distribution
7. Scientific knowledge-nutrition education
8. Food fashions-advertising
9. Food fads—a social phenomenon
10. Custom
    a. racial
    b. national
    c. religious
    d. traditional
11. Food etiquette-preparation, service and manner of eating food

Internal Environmental Influences

1. Hunger (physiological) and Appetite (psychological)
   a. stimulation of sense organs
   b. influence of drugs-insulin, hormones, amphetamine sulfate
2. Developmental pattern-infancy
   a. Inherited emotional and possibly biochemical constitution
   b. satisfaction of instinctive drives
   c. pleasure from the act of eating
3. Parental attitudes toward eating in childhood
4. Physical status, age, sex, intelligence
5. Psychological conditions
   a. inertia-fear of change
   b. emotional setting
   c. memory association
   d. emotional condition-apathy depression, elation, anxiety
   e. food symbolism-security, power, prestige, friendship
6. Physical conditions
   a. work and fatigue
   b. sexual excitement
   c. growth, pregnancy, lactation
   d. allergy and intolerance
   e. disease

mealtime, the desire to eat may be entirely suppressed on contact with obnoxious odors. Hunger, however, is not affected unless nausea is present[5]. Hunger and appetite may also be influenced by insulin and various drugs such as amphetamine sulfate, through their action on postulated hunger and appetite centers in the brain[6].

In addition to these components, there is evidence that food behavior is coincident with specific autonomic nervous activity. Autonomic balance, in turn, may depend on inherited emotional and biochemical constitution. When sympathetic response predominates, certain typical personality characteristics are present, among which are emotional excitability, impatience, relatively easy fatigability and poor food habits. Thus sympathetic hyperactivity may be the prelude of an inadequate diet rather than its sequel.

"Habits" concerning food are laid down in earliest infancy when food not only satisfies the instinctual drive of hunger, but provides oral gratification through the pleasurable act of eating. All openings of the body are important emotionally, the mouth being one of the most expressive. It is related to the major instincts and passions; not only self-preservation, but cognition, love and hate[8]. To the infant the mouth is particularly important, for through it, he satisfies his impulsive and pleasure-seeking desires. Likewise, the first impressions of the physical and social world are gained from early feeding experiences with the mother. Self-confidence and affection on her part develop a sense of security in the infant and enhance his opportunities for growth and well-being. Subsequently in the course of development, certain eating restrictions, principally weaning, are imposed, and new foods are offered to the child. Normally they are adopted in order to conform to adult standards. A flexible attitude toward food usually results. However, rejection of them or sidetracking them, due often to misguided parental education, results in poor food habits[9]. Imitation of parental attitudes toward food and other childhood memory associations with food are also significant criteria in the formation of food habits[10]. Such expressions as "I dislike eggs" or "I hate milk" can usually be traced back to parental sources, either identification with or hostility toward one or both parents.

A poor developmental pattern concerning early nutritional experiences is often manifested in functional disorders in later life, particularly those of the gastrointestinal tract including anorexia, obesity, ulcer, constipation and diarrheal disturbances. This bodily system is most frequently used to express repressed emotions because of its abundant supply of autonomic nerve fibres and because it is symbolic of sustenance and security. Infantile behavior patterns concerning alimentation and excretion, become lodged in the subconscious mind, and at any time may be substituted for mature outlets in speech and action via autonomic innervation[11].

The upper end of the tract is particularly suitable for expressing conflicts concerning receptive trends. Anorexia signifies a decreased intake of food due to loss of appetite and in some cases, loss of hunger sensations. Of course, carcinoma of the stomach, fever, renal disease and alcoholism are common etiological factors. However, in a great many instances, anorexia is a symptom of psychoneurosis, a modification of the severe clinical syndrome of anorexia nervosa. In the latter case, sexuality has been repudiated. The unattractive, emaciated appearance of the adolescent girl, resulting from a prolonged "hunger strike", is a defense against social contacts with the opposite sex. Eating often symbolizes impregnation. Therefore food is rejected. Here psychic rehabilitation takes precedence over nutritional and hormonal therapy. The goal is re-education of the patient toward a mature acceptance of the feminine role. Fortunately the fully-developed syndrome is relatively rare. However, in both men and women, poor appetite is often based on the same psychogenic mechanism—loss of appetite for life. Vomiting attacks may come in this category also, and when no other cause is apparent they often represent repressed sexuality and hostility.

Numerous accounts of obesity in recent literature attest to the significance of psychological as well as nutritional therapy. Probably 90 per cent of overweight is primarily due to emotional maladjustment. Therefore, special diets and weight-reducing procedures will have no lasting value unless the patient can better adjust to himself and his environment. Amphetamine sulfate, the new substitute for will power, has proven effective in curbing appetite. But as soon as the administration of this drug is stopped, appetite is renewed and weight is gained. Obesity signifies overemphasis on oral gratification, food being substituted for mature sexual and social adjustments. The following brief account comes in this category and also illustrates concomittant involvement of another bodily system. A male, aged 49, was first seen with complaints of polyphagia, polydipsia, polyuria, recurrent bilious attacks and headache. The patient weighed 318 pounds. Both parents were overweight and had diabetes. Two brothers each weighed over 200 pounds. A diagnosis of obesity, diabetes, calculus cholecystitis, migraine and recurrent genitourinary infection was subsequently made. The family history of overweight is probably indicative of early glandular disturbance and consequent physiological retardation of genital development. A Rorschach test on this patient revealed that awareness of his genital inadequacy dated from early childhood and there was marked hostility toward his father's greater power as expressed in urination rather than sexual potency. A feeling of inferiority, derived from guilt concerning masturbation, had also been transferred to the kidneys. Finally, there was definite evidence that a large stomach had been substituted for a large genital organ, and that food, symbolizing oral gratification, had been substituted for sexual satisfaction. In this instance there is an obvious need for intense psychotherapy as well as nutritional and medical treatment. The patient is helped to face his early anger and resentment toward the father. His demand for food is minimized through helping him to recognize the reasons why he has substituted eating for sexual satisfaction.

One of the most obvious psychosomatic relationships is the ulcer conflict in which the stomach or duodenum, via autonomic nervous system imbalance, vainly attempts to compensate physically for psychic anxieties. This syndrome develops from an unconscious longing for dependence and at the same time an assertive reaction toward independence. The fundamental pattern is initiated in early childhood where security is sought through striving to conform to overexacting parental standards. Creative urges have to be repressed in order to do what is expected by the parents and resentment inevitably occurs[12]. Recent personality studies on three ulcer patients have revealed in each instance, a basic inferiority due to fear of sexual drives. Childhood restrictions in this area are evident and all aggressiveness has been transferred to the intellectual level. The gastrointestinal tract has taken over the function of expressing libidinal drives.

In the treatment of ulcers, the emotional reactions of the patient are probably as significant as the diet and drugs administered. On the one hand, it is possible for these procedures to provoke an anxiety-producing situation in which their beneficial effects may be nullified. On the other hand, nutritional therapy itself

may serve a psychotherapeutic purpose. The frequent ingestion of milk and cream does more than neutralize free acid. It satisfies an emotional need for affection and security, milk being symbolic of the mother image. Surgery, principally vagotomy, although bringing about a cure for the ulcer, does not insure gratification of these needs, since a food regime is no longer physically necessary. Perhaps the recent advice concerning the postoperative ulcer patient is particularly apt—"Weaning should not be abrupt"[13].

The lower end of the gastrointestinal tract is especially adapted to express retentive and giving tendencies in the individual. Chronic constipation is often a reaction against the obligation to give. In some cases it may symbolize anxiety about offending. In chronic diarrhea and ulcerative colitis, the strong emotional value attached to the feces in childhood may never have been sufficiently given up. In the event of prolonged guilt or anxiety, this infantile pattern is reverted to once again[11]. Impaired nutritional status always occurs with these disturbances. However, rehabilitational procedures should be accompanied by, and often based on psychotherapy.

Nutritional therapy should not be used as a medical discipline, particularly insofar as diet is concerned. First, it may have a variety of conscious and unconscious meanings to the patient, if the physical condition has significant psychosomatic connotations—that is, either specifically related to psychological conflicts or aggravated by anxiety and tension. Prescription diets and vitamin placebos, along with platitudes, may serve to perpetuate a neurosis through fixation of symptoms[14]. Adherence to a dietary regimen may fulfill the patient's desire for self-punishment or may serve to explain away his shortcomings. On the other hand, the patient may find it difficult to follow a certain diet due to reluctance to give up his accustomed eating practices. Every individual clings tenaciously to his foodways and a change in them is a pleasure-reducing task. Therefore, it is rejected. Also a deep resentment may develop due to the nonconformist attitude the individual feels he has to assume before other people. If the diet is violated, guilt feelings come to the fore and may in some cases precipitate the return of physical distress. If this type of person can be helped to accept a new food pattern emotionally and is assured that occasional departures from it will probably have no catastrophic after-effects, he will more readily accept his dietary limitations.

Secondly, and in the light of an integrated concept of nutrition with its multiple conditioning factors, the misuse of nutritional therapy may precipitate or aggravate an already existing nutritional deficiency. The inadequacy of the printed diet lists now in vogue is a prime example. In a single year, six million reducing diets were requested from one pharmaceutical house alone[15]. Granting that they are scientifically accurate, which many of them are not, it is obvious that they cannot fit the specific psycho-social situation of the individual as well as his particular physical needs. The problem of including or excluding fat in therapeutic diets has caused the physician no little concern. Until recently, comparatively little has been known about the role of fat in general metabolism. However, at the present

time, it is no longer considered a final storage form of excess food which can only be burned and converted to carbon dioxide and water, but is regarded as a part of the great metabolic pool of the body, and as such, is available for carbohydrate and protein synthesis[16]. In addition to this role in interconversion with other classes of foodstuffs, fat slows down peristalsis of the stomach, producing a desirable and sometimes undesirable sense of satiation. The feeling of postprandial fullness can no longer be blamed on its indigestibility, however, since all fats, fatty foods and fried foods, either animal or vegetable in origin, are equal if not superior to protein and carbohydrate in digestibility[17], 93 to 98 per cent being utilized by the body[18].

Perhaps of more immediate interest to the physician and surgeon is the management of the postoperative patient, whose nutritional requirements are greatly increased. Adequate water and mineral balance is essential. The liver's total potassium content, for instance, is substantially decreased and the administration of potassium chloride as soon as urine output is assured, obviates the muscular weakness, cardiac enlargement and high venous pressure associated with a deficiency of this nutrient. The necessity for an adequate supply of carbohydrate is well-known. However, if the B group of vitamins are not given also, carbohydrate metabolism is interrupted and pyruvic acid accumulates, acting as a poison. This gradual form of anoxia is first evident in nervous tissue, since it is twenty times more sensitive to oxygen than any other tissue and derives its energy almost entirely from carbohydrate[20]. The common postoperative symptoms of apprehension, irritability, depression, etc. can be alleviated substantially by the administration of thiamine, riboflavin, and niacin in the proper therapeutic proportions. Parenteral protein nutrition concerns blood, plasma, albumin or various protein hydrolysates. Enthusiasm for the latter has run very high of late and it has become important to evaluate the various products on the market in order to give the patient the best preparation at a minimum cost. Several points should be borne in mind. In the first place, all ten essential amino acids must be present, because lack of any one means that the others are poorly utilized or excreted, resulting in negative nitrogen balance[21]. Secondly, the biological value of the original protein, the bacterial purity and lack of toxicity of the final compound should be assessed[22]. A concentrate containing a high nitrogen and low ash content is preferable because it helps prevent nausea and diarrhea. The protein sparers, carbohydrate and fat should likewise be included in order to provide adequate calories. The consequences of misdirected nutritional therapy are nowhere more evident than in the surgical patient. Perhaps, these few illustrations will serve to outline the importance of judicious nutritional supply in the event of an obviously increased requirement for nutrients.

Summary

A variety of external and internal factors may adversely influence nutritive balance in disease and surgery. The clinical application of known facts about food habits and psychosomatic reactions, two of the conditioning factors, may

beneficially supplement preventive and therapeutic nutritional therapy in psychosomatic gastrointestinal disorders.

REFERENCES

1. Kruse, H. D. L.: The Place of Nutrition in the Relationship Between Environment and Health. Milbank Mem. Fund Quart. **26**:41, (Jan.), 1948.
2. Harris, S. C., Ivy, A. C. and Searle, L. M.: The Mechanism of Amphetamine-Induced Loss of Weight. J.A.M.A. **134**:1468, (Aug. 23), 1947.
3. Schneider, D. E.: The Growth Concept of Nervous Integration. J. Nerv. & Ment. Dis. **105**:124, (Feb.), 1947.
4. Goetzl, F. R. and Stone, F.: Diurnal Variations in Acuity of Olfaction and Food Intake. Gastroenterology. **9**:444, (Oct.), 1947.
5. Ginsberg, R. S., Feldman, M. and Necheles, H.: Effect of Odors on Appetite. Gastroenterology. **10**:281, (Feb.), 1948.
6. Grossman, M. I., Cummins, G. M. and Ivy, A. C.: Effect of Insulin on Food Intake After Vagotomy and Sympathectomy. Am. J. Physiol. **149**:100, (Apr.), 1947.
7. Wenger, M. A.: Preliminary Study of the Significance of Measures of Autonomic Balance. Psychosom. Med. **9**:301, (Sept.-Oct.), 1947.
8. Binger, C.: Personality and Oral Disease. Ann. Dent. **4**:175, (Mar.), 1946.
9. Bromberg, W.: Emotional Immaturity and Antisocial Behavior. J. Clin. Psychopath. **8**:423, (Jan.), 1947.
10. Selling, L. S. and Ferraro, M. A. S.: The Psychology of Diet and Nutrition. W. W. Norton and Co., Inc., New York, 1945.
11. Weiss, E. and English, O. S.: Psychosomatic Medicine. W. B. Saunders Co., Phila., 1943.
12. Zane, M. D.: Psychosomatic Considerations in Peptic Ulcer. Psychosom. Med. **9**:372, (Nov.-Dec.), 1947.
13. Szasz, T. S.: Psychiatric Aspects of Vagotomy: A Preliminary Report. Ann. Int. Med. **28**:279, (Feb.), 1948.
14. Halstead, J. A.: Functional Gastrointestinal Disorders: Lessons Learned from Military Medicine. New England J. Med. **235**:747, (Nov. 2), 1946.
15. Editorial: Nutrition and Dietetics in Medical Practice. J. Am. Dietet. A. **23**:875, (Oct.), 1947.
16. Editorial: Fat Metabolism. J.A.M.A. **134**:367, (May 24), 1947.
17. Editorial: Digestibility of Fat. J.A.M.A. **132**:388, (Oct. 19), 1946.
18. Elvehjem, C. A. and Krehl, W. H.: Imbalance and Dietary Interrelationships in Nutrition. J.A.M.A. **135**:279, (Oct. 4), 1947.
19. Metabolic Changes in Diabetic Acidosis. Nutrition Reviews. **5**:315, (Oct.), 1947.
20. The Evaluation of Vitamins in the Practice of Medicine. Philadelphia Med. **43**:661, (Dec. 27), 1947.
21. Editorial: Nitrogen Balance. J.A.M.A. **133**:247, (Jan. 25), 1947.
22. Homburger, F.: Use of Protein Hydrolysates by Mouth. Am. J. Med. **3**:430, (Oct.), 1947.

Discussion

Dr. M. Murray Peshkin (New York, N. Y.):—I rather enjoyed listening to this morning's papers, but my main concern is with the subject of allergy in relationship to gastrointestinal disorders.

I think Dr. Tuft should be complimented for the courage of accepting the challenge to read a paper and discuss it in a very fine manner, because, as you all know, the fur begins to fly and fireworks begin to go when one talks about allergy, particularly of the gastrointestinal tract.

Some of the statements I am going to make have already been stressed by Dr. Tuft, but because of their importance, I think they bear repetition.

Allergy of the gastrointestinal tract affects persons of any age, literally from the cradle to the grave. The most frequent food offenders are those most commonly eaten and the symptoms occur frequently or daily. When the offenders are foods less commonly eaten, the symptoms are more easily traceable to the food, if you think of allergy. Symptoms may occur soon after eating the food or up to 36 hours

later. Symptoms of food allergy must be reproducible by feeding experiments to prove cause and effect. The impression is gained that only food can cause gastrointestinal allergy. The exceptions are those few cases, especially observed in children who suffer with enterospasm from inhaling pollen only during a pollen season. Dr. Tuft stressed that, and I was glad to hear him say so. They may or may not have hay fever. Specific pollen hyposensitization in these exceptional cases clears up the enterospasm.

Children are positive skin reactors to food allergens more frequently than are adults suffering with comparable allergic ailments. Moreover, the positive skin reaction to food allergens, especially with the scratch technic, have a more direct and significant bearing to the gastrointestinal symptoms in children as compared to adults. When allergy to food causes vomiting, enterospasm and simple colitis, such symptoms are rarely associated with organic lesions in children, whereas in adults long standing neglected or unrecognized gastrointestinal allergy may eventually be complicated by organic or irreversible pathologic changes of the affected tissues.

The important point to emphasize is not how often gastrointestinal allergy occurs but rather that the allergic condition be recognized as early as possible so that appropriate dietetic management can be instituted and the disturbing symptoms eliminated.

Dr. Tuft's warning not to confuse food intolerance with true food allergy of the gastrointestinal tract is well taken and important—but any attempt to minimize the role of foods in intestinal allergy because such foods contain negligible or small amounts of allergenic substances I think is a mistake. I can cite the case of a physician, 60 years of age, who is now and has been for many years, violently clinically sensitive to only raw apple. A pea-size piece of raw apple induces the most distressing gastric symptoms coming on several hours after ingestion and lasts for 1 to 2 days.

I am not so certain that all of the fat and sugar intolerance cases described by Dr. Tuft are nonallergic. Landsteiner's haptenes have taught us that a nonantigenic substance can be made to combine with a protein to form a new substance—a conjugated protein—capable of causing allergic symptoms. Synthetic drugs like aspirin, phenobarbital, etc., are known to cause violent allergic reactions. Yet, they themselves are only haptenes and are nonantigenic. These drugs become conjugated proteins when they come in contact with the tissues. Why not lipoids and sugars?

Most if not all of the patients Dr. Tuft refers to are adults also affected with asthma, hay fever, urticaria or perennial allergic rhinitis. Food skin tests in these patients are most often negative. In fact the diagnosis of allergy of the intestinal tract is not difficult to make when the patient is suffering with other allergic syndromes. However, the patient having symptoms of allergy referable only to the intestinal tract, is another matter and not one easily diagnosed because allergy is not the condition initially suspected. Moreover, the practitioner or gastroenter-

ologist sees almost all of these patients long before the allergist, who, by the way, sees very few of these patients.

Diet trial is the most simple and effective means of diagnosing and treating allergy of the gastrointestinal tract. The most dramatic relief of alarming symptoms are at times observed after the removal of the offending food from the diet.

In this connection I must state that I think we allergists are guilty, without any recriminations, of conditioning more patients to a restricted diet for more years than are necessary. I could spend some time, if I had it, telling you of patients who have been on diets for twenty-plus years and who are afraid to go off them, because they think they will become ill if they eat the food. If they have that much fear of food allergy when the allergy has long burned itself out, they certainly will suffer with this pattern of gastrointestinal symptoms.

I am not unmindful of the influence of the psyche on the soma. It applies to every disease mankind is heir to. Then why not to allergy of the intestinal tract especially when the illness has been of long standing? A complicating disturbed psychology must of course be recognized and appropriately treated.

In the final analysis it is the important task of the physician to recognize that allergy can affect the gastrointestinal tract only. And, the institution of appropriate dietetic measures may result in relief from symptoms.

Dr. W. C. Spain (New York, N. Y.):—Dr. Tuft has quite properly pointed out the difficulty in demonstrating that an allergic factor may be responsible for a gastrointestinal disorder. Often a food intolerance is confused with a specific food allergy. The difficulty in digesting fatty food substances is not an allergy, nor is the inability to handle foods such as egg, poultry or cheese whenever they have been in cold storage overly long. Often too, the attempt to obtain from the patient upon meticulous history-taking, any reliable or helpful information, meets with failure. The skin testing procedure which is so consistently of value in almost every case of respiratory allergy due to inhaled substances, such as pollens, dusts, animal danders etc., is helpful only in one-half or less of the cases of gastrointestinal allergy due to foods.

It is very useful in the consideration of patients with a problem suspected as being due to food allergy to bear in mind that cases of food allergy divide themselves into those that have a very brief reaction time between contact with the eliciting food and the appearance of symptoms, and those with a delayed reaction time. In the first group the symptoms occur within 24 hours or less usually within an hour, and may be sudden, severe and explosive in character, as in the patient cited by Dr. Tuft, the physician in whom the ingestion of corn produced severe diarrhea. In the second group the symptoms occur after an interval of 24 hours or more, are usually protracted, often less intense, frequently obscure. In the first group, skin tests with the specific eliciting food factor are positive as was true of the skin test in the corn allergic physician. In the second group, skin tests, even with the subsequently proven eliciting food factor, are negative; and yet it is in this second group, where the skin test fails us, that the attempt to diagnose by

history, also frequently fails, and we are reduced to the often unsatisfactory employment of trial and error diets. To prove that a suspected food is the specific factor in the causation of a gastrointestinal ailment, we must, as Dr. Tuft states, corroborate any evidence obtained upon history, by successful clinical test; in the immediately reacting group described, the skin test with the food should also be positive. The observance of these requirements greatly reduce the lists of so-called food allergies, and will make any food sensitive group, impressive for its size, hard to come by.

I wish to thank Dr. Tuft for the opportunity of discussing his excellent paper and the National Gastroenterological Association for its invitation to do so.

Dr. David R. Meranze (Philadelphia, Pa.):—It is gratifying to a pathologist that such a paper as Dr. Madden's has been presented to clinicians. The work reported is in line with an emerging trend which points to the importance of nutrition in general and protein nutrition in particular, for many of the conditions which clinicians are called upon to treat and prevent.

Already much has been achieved: the more adequate preoperative and postoperative care of the surgical patient, with its probable reduction in postoperative infections and complications; the more rapid healing of wounds and fractures; the more rational treatment of the hypoproteinemic state and the anemias; the contribution to the overall welfare of the pregnant woman and the hyperthyroid; and the insight into the antibody response of the organism.

In these and in related matters the physiologists, the physiologically-oriented surgeons, and such physiologically-oriented pathologists as Dr. Madden, have made major contributions.

The lag of the clinicians in applying these data to their fields of activity is apparently being made up. Thus, in Philadelphia a group of us, including the Doctors Wohl and Dr. Perchonock, have begun the determination of the plasma protein levels in diabetics, and the investigation of the relation of these levels to the diabetic state and its complications. In a routine study we have found an appreciable number of diabetics with low normal and subnormal plasma protein values. In view of the probable correlation of such values with a depleted tissue protein pool, and in view of the implications which such a probability entails, our observations may prove of significance in the treatment and prophylactic care of the diabetic.

The data which Dr. Madden has presented this morning represent one level of precision. They have already found rich applications in the past and promise more in the future. I should like to direct your attention to possibilities at other levels of investigation, to which I hope clinicians will become equally attuned. The protein nutritional needs of an organism are not only a function of its own internal growth characteristics and its varying vissicitudes of health and disease, but also are conditioned by its continuing past, namely, by the effects of the differing dietary patterns in various nationalities, social groups, and those resulting from differing culture habits.

In such a variable and changing nutritional environment I would point to the pertinence of Spiegelman's work on the adaptive and constitutive enzymes. This work demonstrates the emergence and disappearance of enzymes under varying conditions of need, and indicates the competitive effects on other enzymes present, in the presence and even in the absence of their specific substrates.

Again, superimposed on a homeostasis, grounded in a dynamic protein pool, and an interchange at the amino acid level, with its protein priorities in production and utilization, there may be postulated another dynamism at the cytostatic level. The work on the ribose- nucleo-protein and desoxyribose- nucleo-protein patterns in the cell, made possible by the histochemical technics of Brachet and others, brings us to the very frontier of intracellular flux, and makes contact with basic varieties of protein.

The pathologist of the past, because of the limitations of available technics, has necessarily been preoccupied with the structural aspects of protein metabolism. He and the physiologist are, by virtue of the newer technics, now in a position to explore with some precision the functional aspects of protein metabolism, a task which the work reported by Dr. Madden has furthered and for which it has provided a base. The accruing results are almost certain to be as rewarding to the informed clinician.

Dr. Thomas H. McGavack (New York, N. Y.):—I was asked to discuss the portion of this symposium concerned with Dr. Biskind's presentation. I must say I am much in accord with Dr. Biskind's efforts to bring together the vitamin and hormonal fields of investigation and therapy.

In his opening, Dr. Biskind remarked that the endocrine disturbances he has observed are secondary to some one or more phases of an altered vitamin metabolism.

Here, I would raise the first question in relation to Dr. Biskind's paper. Is it obligatory that we recognize the gastrointestinal manifestations as always primary and the endocrine symptoms as secondary? One illustration may be to the point. The metromenorrhagia that we often see, sometimes associated with other disturbances which could be looked upon as of a nutritional nature, may completely yield to the action of small doses of testosterone; moreover many of the accompanying gastrointestinal and other disturbances may simultaneously disappear. Perhaps a more dramatic example may be pertinent. Dr. Biskind has shown several cases in which severe gingivitis and glossitis existed, and which he has attributed to lack of vitamins and too much estrogen. We have seen clinically indistinguishable cases, in which the adequate therapy proved to be estrogen alone. Such conditions were obviously not instances of a hyperestrinism secondary to hypovitaminosis, but hypoestrinism which, when relieved completely, caused the secondary oral condition to disappear.

Many of these can be distinguished from a great number of Dr. Biskind's patients on the basis of their temporal relationship to the menstrual cycle, while

in other instances, either a vitamin deficiency or an estrogen lack may produce irregularity of menstruation.

The next question is in connection with cirrhosis of the liver. Does the body build of some of these patients have any relationship to the background of their disturbances in vitamin absorption and utilization? That is, do we start with an abnormal constitution or, if you like, with certain endocrine factors ajar, which, in turn, interfere with the individual's usage or failure to use certain vitamins? I think we will all agree that pectoral alopecia, hypogonadism, loss of muscular strength, libido and potency are present frequently in patients with cirrhosis. That they had always existed and invariably represent a constitutional diathesis we certainly doubt, for we have now had an opportunity to observe the course of several patients prior to and after the development of the cirrhotic condition. Some of the most manly specimens with well developed secondary sex characteristics have been stricken with cirrhosis and shown all its attendant alterations in primary and secondary sex patterns.

The behavior of these subjects when subjected to a low vitamin intake and poor assimilation supports Dr. Biskind's major thesis whole-heartedly. However, there remains a large group of individuals who showed constitutional inferiorities of an endocrine nature before the development of the cirrhosis. In these, should we always look upon the vitamin deficiency as primary to the development of the cirrhosis and its attendant endocrine disease, or can it be that some other factor is primary, allowing the vitamin disturbance to act as an incidental and exciting cause?

That question arises in connection with vicious cycles which may appear in the interactivity among gastrointestinal function, hormones and vitamins. For instance, it is known that estrogens in large doses depress the activity of cholecystokinin, and thereby depress a factor concerned in the absorption and availability of certain vitamins to the body. Such interaction can initiate and maintain a vicious cycle of events.

Dr. Biskind chooses to break this vicious cycle only with vitamins. I am wondering if it wouldn't be wise to break it in two directions, not only with vitamins but also by some substance which can suppress estrogenic activity. Small doses of testosterone would so act.

Dr. Biskind mentions the redistribution of fat and the disturbances of insulin activity that sometimes occur, and that seem to be relieved by supplying certain vitamins. I wonder if we are forgetting that the gastrointestinal tract is perhaps the most important single endocrine organ in the body, producing at least twelve well-recognized endocrine materials, and possibly others.

In this particular connection, since Dr. Biskind has mentioned insulin, the substance called duodenin or incretin,—or both of them, if you think they are separate hormones,—with its ability to produce vagal stimulation, and its ability to produce hypoglycemia—may initiate or aggravate these disturbances of which he speaks.

Again a question for Dr. Biskind: Does he believe, or can he prove, or has he proven in a majority of cases that hepatic dysfunction is always present? If so, I would be interested in his hepatic tests.

The cases in which we have been able to show disturbances of hepatic function in laboratory methods have been chiefly our cirrhotics. In our experiences with them, I think we can verify whole-heartedly practically all of Dr. Biskind's tenets. However, we have not seen the apparent hyperestrinism unless the hepatic dysfunction could be readily demonstrated by laboratory examination, at least by the single specimen multi-test routinely employed by us.

I liked Dr. Biskind's concept of vitamin therapy. Today we know so little about the specific action of each vitamin in relation to other vitamins and to the body as a whole, that it behooves us to utilize well balanced mixtures, including unrefined natural fractions of liver which contain trace substances the exact nature of which we do not yet know. However, they certainly seem to be as important as the substances we have been able to study carefully, of which we have learned the chemical formulae, and which we can obtain in a crystalline form. In connection with therapy, there is one further question. Why, Dr. Biskind, has it been necessary for very protracted periods of time to maintain these people on five to ten times the amount of material that the normal person needs? Does not this in itself suggest that some factor other than vitamins is concerned in the conditions Dr. Biskind has discussed?

Dr. S. William Kalb (Newark, N. J.):—Dr. Kelly has ably stressed the fact that habits are laid down in infancy. Various types of diets depend upon envioronment; different religious and racial groups have dishes for which one yearns when he matures. These often constitute a one-sided diet. In some races carbohydrates are the dominant factor; in others fats, and in still others protein. A uniform or balanced diet is not adhered to and, as a result, education such as Dr. Kelly stressed must be resorted to until these habits become more adjusted.

In a small number of cases for a limited time we find that either environment or heredity plays a part. Sometimes we wonder whether there isn't another factor involved, namely self-control. There is a wide gap between the minimum diet which prevents deficiency symptoms, and the optimum to promote good health.

Dr. Peshkin stressed here today that allergy diets are common causes of deficiency diseases. We know that we often give patients a gallbladder diet or an ulcer diet, which also causes deficiency symptoms. The fear of these patients, as Dr. Peshkin stressed, is one of the reasons why we have so many vitamin deficiencies. Then again, following surgery, the patients' trays are taken away most of the time in the same manner in which they are brought out. There isn't strict enough supervision to see that the patient partakes of the contents of the tray.

It is safe to assume that emotional maladjustment accounts for most of the obesity. The drugs in use today are not satisfactory to overcome these factors. Amphetamine sulfate inhibits the appetite in a small number of cases for a limited time.

Dr. Kelly stressed today the physiological difference between hunger and the emotional difference of appetite. I don't know where to draw the line on amphetamine sulfate between hunger and appetite. I know in my experience we ran a series of over five thousand cases on amphetamine sulfate and we were not able to control appetite in more than about 20 per cent of the cases, and then only for about a week or two. In continued use of the drug over a long period of time the appetite returns to normal. The patients still continue to have their emotional stimulation but along with it many side reactions.

Now, if a new brand of amphetamine sulfate is coming out which will not produce the nervous manifestations and the insomnia resulting from the drug, and if it will be able to control appetite for a longer period of time, so much the better. However, in the treatment of obesity up until this time we still don't have any drugs that can be relied upon exclusively.

The gastroenterologist has been using diets longer than any other group of practitioners in medicine. Yet it has been the province of the biochemist to come to the fore to teach us how to use drugs and foods for nutritional therapy. It behooves this group and all men doing gastroenterology to pay more attention to biochemistry and to its effect upon nutrition.

I want to thank Dr. Kelly for his paper. It was so complete that it was very difficult to find anything else in nutritional therapy to add to it.

Dr. Louis Tuft (Philadelphia, Pa.):—Dr. Spain and Dr. Peshkin were kind enough to emphasize most of the facts brought out in the paper. I have very little to add except to say that I agree with Dr. Peshkin that perhaps fat intolerance or fat and sugar intolerance is an allergy and, as I mentioned, possibly due to one of the split products.

It is true that a food or a substance does not necessarily have to be of a protein nature to produce an allergic reaction. Drugs are a good example as well as various other chemicals but as yet we cannot prove that fat intolerance is upon an allergic basis. It may be an aldehyde, or it may be one of the split products of the sugar itself, but until such proof is obtained, I think it would be better to label the condition as fat or sugar intolerance rather than fat or sugar allergy.

While most of the patients that we have seen have been allergic, Dr. Tumen, who studied these cases with me, has also seen similar conditions in patients who were not allergic, so that the condition does appear in allergic or nonallergic individuals alike.

Dr. Morton S. Biskind (New York, N. Y.):—I am grateful to Dr. McGavack for emphasizing some of the complicating factors; in fact, he brought out so many of them, I doubt whether we could cover them all in the rest of the afternoon. Certainly, as he pointed out, the gastrointestinal manifestations are not necessarily primary.

Dr. Kelly discussed some of the psychogenic factors which are unquestionably extremely important, and then, there is the whole series of other contributing factors, so-called "conditioning" factors, such as the use of various drugs, excess

physical activity, excess consumption of carbohydrates, and the like, all of which can initiate nutritional deficiency and secondary endocrine disturbances.

As to the relation of constitutional factors to the occurrence of nutritional deficiency, I am certain that this is an important subject. We know even in working on rats, for instance, that one strain, the Sherman strain, is highly susceptible to nutritional impairment of hepatic function, while the Sprague-Hawley and Long-Evans strains are much more resistant. That this occurs in human beings also is very likely.

As to the use of hormones together with vitamins in the treatment of some of these conditions, there are occasional instances in which small doses of estrogen or androgen would be indicated, and do produce additional improvement. We rarely use them in these cases and for the most part have found them unnecessary. Of course, in using androgens, one neutralizes the excess estrogen at a higher absolute level; by giving nutritional therapy the normal estrogen-androgen ratio is re-established at a physiologic level.

The effect of estrogen on other hormones and on the various vitamins, is something about which, as yet, we know very little. In addition to the effect on cholecystokinin, that Dr. McGavack mentioned and which I had not previously known, Ashworth and Sutton demonstrated some years ago, that administration of estrogen can produce lesions of nutritional deficiency. This effect occurs presumably through the destruction of the B vitamins in the process of inactivating the estrogen.

About hepatic function tests, we have found no correlation whatever between the usual hepatic function tests and the occurrence of syndromes related to excess estrogen. If it were not such a difficult and laborious procedure to do the sort of thing that Glass and his collaborators did some years ago on cirrhotics, namely, to determine the ratio between free and combined estrogen in the urine, this might turn out to be the most sensitive liver function test we could have.

Zondek did something similar—the so-called "estrone clearance" test. He did not determine the ratio of free and combined estrogen, but merely the amount of estrogen recoverable from the urine.

Now, as to the necessity of maintaining patients who have been nutritionally deficient on at least five to ten times the amounts of the various vitamins that a normal person can get along on, once the avitaminotic lesions are healed. I don't know the explanation for that phenomenon except that I know it is so. Dr. McGavack may well be right in suggesting that there are certain as yet unidentified nutritionally essential substances which when therapeutically available would permit the tissues better to retain the vitamins once an avitaminotic lesion is healed. Bessey and Lowry showed, for instance, that the same thing occurs in animals. They studied the riboflavin content of the rat cornea, and they found that if the rats were depleted in riboflavin, the amount in the cornea was reduced accordingly, but if they then added riboflavin to the diet they could not restore the original amount of riboflavin in the cornea. The cornea somehow lost its ability to take

up the amount of riboflavin originally present, and this apparently irreversible phenomenon undoubtedly accounts for the situation we see in the human being.

Dr. Herbert T. Kelly (Philadelphia, Pa.):—I should like to thank Dr. Kalb for his gracious discussion and acceptance of some of the facts presented.

In closing I should like to make a plea that we endeavor to integrate nutritional, medical and psychogenic factors in order to realize rehabilitational goals.

URETHANE THERAPY IN LEUKEMIA*†

ADOLPH J. CRESKOFF, M.D.
and
THOMAS FITZ-HUGH, JR., M.D.
Philadelphia, Pa.

In April, 1946, Haddow and Sexton[1] reported the use of certain carbamic esters in experimental rat cancer. Ethyl carbamate (urethane) yielded results superior to those of any other compound of this group. It alone produced not only growth inhibition but also fibrous replacement of the cancerous rat tissue. For this reason, the drug was tried in human subjects with breast and other malignancies. The results proved disappointing but it was observed that some of the patients developed leukopenia. This observation then motivated the first trials of the effects of urethane in leukemia and certain other lymphadenopathies.

In May, 1946, Paterson, Haddow, Thomas, and Watkinson[2] reported on the results of urethane therapy in 32 cases of leukemia. The usual dose was 3 to 4 grams daily. The cases responding favorably were quite comparable with cases receiving standard x-ray therapy. No intimations of cure were made.

Of Paterson's 32 cases, 19 were classed as myelogenous leukemia. Of these, 8 received considerable benefit from urethane alone: that is, a state of clinical as well as hematological remission occurred and was maintained for a reasonable period. These patients improved symptomatically; their spleens shrank markedly and a more or less prompt fall in the total number of leucocytes occurred together with approach of the differential cell count to normal values. Less favorable response labelled "improved but unsatisfactory" were noted in four other cases of myelogenous leukemia. In three others urethane failed, but did not inhibit nor affect consequent favorable response to x-ray therapy. Four patients died during urethane medication; one of these being classed as an acute leukemia. Similarly, 13 cases of lymphatic leukemia were treated. Two cases responded well and 2 others had only fair responses from urethane alone. In 5 additional cases it was deemed necessary to supplant urethane therapy with x-ray treatment either because of intolerance to the drug or failure of adequate responses. Four cases of lymphatic leukemia died during urethane therapy, one of these being classed as acute.

The most frequent toxic effects noted by these workers was nausea, at times severe; drowsiness; diarrhea; anorexia; and in 2 cases evidence suggesting hypoplasia or aplasia of the hematopoietic system.

On the basis of the report by Paterson, parallel observations were started at the Hospital of The University of Pennsylvania in June, 1946. To date a total of 19 cases of all types have been treated. These cases include 5 of chronic myelogen-

*Abstract of a paper read before the Twelfth Annual Convention of the National Gastroenterological Association, Atlantic City, N. J., June 4, 5, 6, 1947.

†From the Hematology Section of the Medical Clinic of the Hospital of The University of Pennsylvania.

ous leukemia, 7 of chronic lymphatic leukemia, and 7 of acute leukemias or various types. It is emphasized that of our 19 cases, 10 were unfavorable for any kind of known treatment: that is, 7 were cases of acute leukemia, and 3 were chronic cases in terminal "x-ray resistant" relapse. Our average dose was 4 grams daily given in solution by mouth. The range of dose was 1 to 8 grams daily. In responsive cases the time required for a definite hematological response averaged 48 days. In the acute cases a fall in the white count was seen more rapidly (8 to 14 days). In a few cases urethane was variously administered by rectal suppositories, orally in capsule form, and locally in ointment form. In one case we are administering urethane intravenously.

Of the 5 chronic myelogenous leukemias, 1 attained an excellent result. This patient, a 30-year old white female presented herself with an initial leukocyte count of 212,000/cmm. and a hemoglobin of 8.35 grams (53.5 per cent). The spleen descended to the iliac crest. At the end of 35 days of treatment with 3 to 4 grams daily, the white count was 13,400 and the hemoglobin 12.56 grams (80.5 per cent). The spleen regressed in size until it was palpable only 4 cm. below the costal rim. It was interesting to note that this patient became pregnant during the later stages of treatment and is at the present time successfully entering her 4th month of pregnancy. Of the remaining 4 cases, 3 were patients who had had the disease for some time (1 to 5 years), and had received several courses of x-ray therapy, and at the time of inception of urethane treatment were judged to be in terminal relapse. In each of these cases there was a marked drop in the leucocyte count after urethane, without accompanying clinical improvement. One remaining case has received urethane intravenously for so short a time that evaluation at the time of writing is impossible. In summary: of 2 patients with chronic myelogenous leukemia, treated with urethane alone, 1 has had an excellent response; 1 is too early for evaluation.

Of the 7 cases of chronic lymphatic leukemia, 2 showed excellent results. One patient whose initial count was 605,000 WBC/cmm. received a total of 243 grams of urethane over a period of 72 days. At the end of this time the patient was clinically well, and there had been marked regression in the size of all lymph nodes and particularly in the size of her spleen. This patient has now enjoyed 8 months of remission without any therapy and shows no signs of impending relapse. Her differential count has reverted to approximately normal values for lymphocytes and granulocytes. Four patients with lymphatic leukemia had partial and unsatisfactory responses. One responded hematologically but without clinical improvement and is judged as a failure. Of the 4 cases with partial responses, 2 are still receiving urethane and 2 have been transferred to x-ray therapy. It is interesting to note that a full course of x-ray therapy in these latter two patients has also failed to achieve an optimal therapeutic effect.

None of the 7 cases of acute leukemia has survived. In one patient with acute monocytic leukemia an apparent remission of several months duration occurred. Not only did the peripheral blood picture improve, but bone marrow aspirations before and following therapy showed almost complete disappearance of blast forms

from the marrow. In another case (acute myeloblastic leukemia) it was felt that a surprisingly good remission was under way when the patient died suddenly of pulmonary embolism from phlebothrombosis. One child with leukemic masses involving both kidneys showed marked clinical and x-ray evidence of reduction in size of the tumors prior to death. The remaining cases were treated intensively without discernible effect upon the swift course of the disease.

Our experience with the toxicity of urethane is that nausea is the predominant symptom and is seen in about 50 per cent of cases receiving the drug. Occasionally, nausea was severe enough to necessitate reducing or stopping the drug. Less frequent toxic effects were sweating, drowsiness, and anorexia. There is evidence in 2 of our cases that heavy dosage with urethane may have contributed to production of hypoplastic marrow changes.

In order to compare our results with those of standard x-ray therapy, it is necessary to exclude certain of the cases in our series from consideration; that is, all acute leukemias and three chronic cases which had lived the leukemic span of life under x-ray therapy and were terminal when urethane was started.

Of the remaining 8 cases, 3 attained excellent remissions; 2 others have shown fairly good results and are still under treatment. A fifth case has received so far only a few doses of intravenous urethane and evaluation is impossible. Of the remaining 3 cases, one patient died during therapy although he had obtained an apparently excellent hematological response. This patient was elderly and had had recent prostatic surgery in addition to a single incomplete course of x-ray therapy some months prior to urethane therapy. The final 2 cases showed a certain degree of hematologic and clinical improvement after long courses of urethane but were transferred to x-ray therapy because of incomplete responses. It is interesting to note that these two cases responded suboptimally to full courses of irradiation.

It is our impression from this small group of cases that urethane will prove to be an excellent adjunct in the treatment of chronic leukemia. It is impossible at this time to state whether this drug is more effective in one form of chronic leukemia than in another. Nor is it possible to anticipate which case will respond and which will fail to respond. No information is available as yet as to whether a full series of remissions produced by urethane can then be followed by an equal number of remissions induced by x-ray therapy. If this should prove to be so, then prolongation of life as well as symptomatic improvement may be possible in victims of leukemia. Our results with urethane are as promising as those obtained by Paterson and her coworkers. We feel that urethane should be recommended for further trial in the treatment of leukemias of all types.

BIBLIOGRAPHY

Haddow, Alexander and Sexton, W. A.: Influence of Carbamic Esters (Urethanes) on Experimental Animal Tumors. Nature, London. **157**:500-503, (Apr. 20), 1946.

Paterson, E., Haddow, A., Thomas, I. A. and Watkinson, J. M.: Leukemia Treated with Urethane Compared with Deep X-ray Therapy. Lancet. **1**:677-682, (May 11), 1946.

DISCUSSION

Dr. Max M. Strumia (Bryn Mawr, Pa.):—In the appreciation of the effects of any therapeutic means for the treatment of leukemias many of the old standards

must be looked upon in a somewhat different light. The total leucocyte count, for instance, has diagnostic value and is of some significance when very high. For the values, however, most commonly encountered, that is, about 250,000 or less, the leucocyte count has a minimal significance either as an index to the course of the disease or effectiveness of therapy.

It is quite obvious that if a low leucocyte count were to be of good prognostic significance, all the cases of aleukemic leukemias should do very well. As a matter of fact, there is no difference in the course and in the responsiveness to therapy between leukemic and aleukemic forms of the same type of leukemia. We have found over a long period of time that much more significance in the evaluation of the course of leukemias and in the evaluation of the effect of therapy is to be placed on the total nitrogen output and the uric acid level, on the hemoglobin concentration, on the platelet count and on the clinical picture as a whole. When these factors are taken into consideration, it may be found that urethane therapy has probably less effect than it would appear if the variation in the leucocyte count is overemphasized. Thus, of 18 cases of chronic myeloid leukemia reported by Paterson and coworkers, after a mean interval of six months with urethane treatment, there was a significant hemoglobin rise in seven cases, no significant change in four and a drop in three, in one case very severe. Four cases had no check-up at the end of the treatment; another case died with symptoms of aplasia of the hematopoietic system for which the drug was held partially responsible. It is to be noted that some of these patients also received x-ray therapy and two received whole blood transfusions.

Of twelve cases of chronic lymphatic leukemia similarly treated, there was a decrease in hemoglobin in four, this decrease being very severe in one case; an increase in three cases; no data in three and doubtful results in two. Some of these patients also had x-ray therapy. In the series of 19 cases presented by Drs. Creskoff and Fitz-Hugh, all cases are very clearly analyzed. As one might expect from the results obtained by other workers, in seven cases of acute leukemia no favorable response was noted. Three cases have been rejected as being in the terminal stage of chronic leukemia, which leaves nine cases for analysis. Of these, eight have been mentioned in the comments; three are considered as having attained excellent remissions, two of chronic lymphatic leukemia and one of chronic myelogenous leukemia; two others have shown fairly good results. On the whole, these results do not appear to be better, if as good as those obtained when diet therapy with high protein feeding is used in conjunction with minimum of x-ray irradiation.

It is my feeling that a comparison of the results obtained with urethane and the results obtained with x-ray treatment should not be made unless the x-ray dosage is known and unless the diet and some knowledge of the nitrogen balance is available. Perhaps the most discouraging part of the presentation is that which refers to the nausea as a toxic side effect of urethane therapy. In most patients suffering from leukemias there is an increased nitrogen loss with resulting hypoproteinemia, which unquestionably plays a very important role in the anemia shown by these patients. It is generally difficult to maintain these patients on a normal

or positive nitrogen balance, therefore nausea should be considered as a very undesirable side effect. Our experience with urethane is entirely too small to comment upon. It was used in patients who had previously received x-ray treatment and who had a more or less stationary course.

The two cases studied were both of chronic lymphatic leukemia. The only effect noted was a relatively small drop in the leucocyte count.

In conclusion, I think we are justified in (1) employing urethane experimentally particularly in cases which do not respond favorably to the standard treatment. (2) Excessive optimism in the final results is probably premature. (3) If nausea occurs, interfering with nutrition, urethane should be discontinued.

Dr. Creskoff and Dr. Fitz-Hugh have presented the best studied series of leukemic patients treated with urethane. It is only after numerous such presentations that a critical appraisal of the effect of urethane therapy can be attempted.

While waiting for more such definite evaluation, it is important to determine whether or not continuance or even expansion of such studies is justified.

Two new remedies recently proposed for the treatment of leukemia, radioactive phosphorus and nitrogen mustard, have not fulfilled the early promises.

The urethane therapy being discussed is more promising and worthy of attention.

Dr. Claude E. Forkner (New York, N. Y.):—I liked this paper because I felt that there wasn't too much enthusiasm about it, and I think that is the way we should feel about this new tool that has been added to the armamentarium against leukemia. I certainly feel, with Dr. Strumia, that it is premature to be enthusiastic about this treatment, and that the experience with it thus far is perhaps not quite as bright as it might look if examined only superficially.

You are familiar with the tools that we have for use in the treatment of leukemia. Irradiation either by x-rays, by radium, or by radio-phosphorus is the one that enjoys the widest reputation. Irradiation has been used since 1903, for about forty-five years, and is still, the best agent that we have in general for the treatment of the various types of chronic leukemia. The subacute and the acute forms respond favorably to no type of therapy.

Then there is the old method of using arsenic, first used in leukemia about 1865, and rediscovered quite accidentally, in 1931, as a valuable agent in the treatment of chronic myelogenous leukemia. Benzol was used by Selling and his associates and given up, perhaps without sufficient reason. I think the evidence for benzol is still pretty good, but everyone is afraid of it because of certain carry-overs in the literature. The newer treatment with nitrogen mustard, is not the method of choice in the treatment of chronic leukemia. In acute leukemia, treatment with nitrogen mustard has produced some remissions. There have been many failures.

This new agent, ethyl carbamate, or urethane, has been used in a relatively small number of cases. No one can draw a final conclusion with regard to its usefulness in acute leukemia. Spontaneous remissions in acute myelogenous and acute

monocytic leukemia are not uncommon. We do not understand the mechanism by which they occur.

None of these agents can be said to cure leukemia. There are cases which closely resemble leukemia of one sort or another, but which have become stationary or have been cured of their disorder, but not by any agent with which we are familiar. It seems to be spontaneous remission and spontaneous cure.

There was one famous patient whom we followed for twenty-five years, and every time she was seen, the persons who saw her thought that she really must die within a period of a few months. That went on for twenty-five years. She did the work of three people and supported her family. She remained quite well without treatment and without progression of her disease for many years. Certain patients will do that sort of thing, so that one is not justified in drawing any conclusions from a small number of cases.

All of these agents must be used with care. The improper use of irradiation—and it is often improperly used—is dangerous. The improper use of arsenic is dangerous, although perhaps not quite as dangerous. Benzol can be improperly used. Nitrogen mustard is dangerous, and ethyl carbamate or urethane, probably has certain dangers. The exact delineation of what cases it should be used in and how it should be used, must await further study.

I feel that one of the most important things which must be done in the study of this agent, as well as with other agents, is to gain a knowledge about the mechanism of how they work. It is surprising that we do not know the mechanism of the control of the white blood cell count and red blood cell count even, in normal men, and actually there has been no systematic study of the blood-forming organs from the standpoint of what governs their hypo- or hyperactivity. That is a rather startling statement to make, but it is true. Dr. Creskoff has told you that it was an accidental discovery which led to the use of urethane as a tool in the treatment of leukemia; so it was also with arsenic, and also with irradiation, and with benzol.

I should like to know what these workers have found with regard to how urethane should be administered. Is it wise to administer it immediately after meals, if given by mouth, or is that of any importance?

In the administration of arsenic, it is important to give it immediately after meals and well diluted. I find most of the mistakes in the use of arsenic are due to the fact that the doctor has not seen that the medicine was given properly.

There are many tricks in treatment, which must be adhered to, and perhaps some of these symptoms of nausea might be overcome if one would pay more attention to just how the medication is given.

When I wrote a book on leukemia about ten years ago, one of the reviewers in the Journal of the American Medical Association said, "It is problematical to us to see how anybody can write so much about a disease concerning which we know so little". I think we know really very little about leukemia, and I shall look forward to this work with ethyl carbamate and nitrogen mustard, not so much because I

think they are going to be of any very striking clinical value in the treatment of leukemia, but rather because they will stimulate work and thought concerning the mechanisms by which we may influence the disease. Through a knowledge of how these agents work, whether it be on the enzyme systems or in other ways, there is an opportunity to acquire more fundamental understanding about the nature of leukemia.

Dr. A. J. Creskoff (Philadelphia, Pa.):—I want to thank my two distinguished discussers and I agree emphatically with their attitude that we must be conservative about this new drug. It is a new tool we are trying in leukemia. We have a great deal to learn about what it will do and will not do. It will drop the white count, but often will not improve the patient clinically.

As to the nausea, which is so distressing, I feel somewhat hopeful about that phase because when the drug is administered intravenously, nausea has not occurred in a total of forty or fifty injections we have given. This means that this drug does not have a central nauseating effect. Enteric-coated tablets of urethane may partly obviate the nausea often present when this drug is given orally. We have found that the drug is best given after a full meal. We have most often dispensed it in a solution which is flavored with a little syrup of orange and chloroform water. Patients have told us that when the dose is taken in a small amount of some carbonated beverage they cannot taste the medicine. It is important to avoid suggesting nausea to these patients in warning them of this possibility.

In conclusion, again I want to thank this meeting for the privilege of presenting this work.

RECENT ADVANCES IN PHYSICAL MEDICINE*

RICHARD KOVACS, M.D.
New York, N. Y.

The use of physical agents in treatment of disease and injury has been instinctive with the human race since early days, and the story of the gradual evolution of the therapeutic employment of the various forms of natural force makes fascinating reading. Curiously enough, "scientific" medicine in the past century was so completely absorbed in progress along basic physiology, pathology, pharmacology and here in the United States especially in the advancement of surgery, that it took comparatively little interest in the advancement of the oldest form of therapeusis, the use of natural or physical agents.

In the United States it took two World Wars and much testing in laboratories and at the bedside until the medical profession has finally taken to employing "physical medicine" as part of the every day practice of medicine. After so many thousand of disabled service men and women and many more civilians were benefited by physical treatment, professors of medicine do not raise their eyebrows any more when the uses of electricity, heat, light, massage and exercise are advised by "regular" doctors.

World War I brought for the first time the organization of full fledged departments of physical "therapy" where all the time honored and many of the newer methods of physical therapy were employed under the watchful eye of interested medical men. Graduate and undergraduate instruction in the subject were gradually inaugurated, replacing the earlier commercialized teaching fostered by some manufacturers eager to unload their wares on gullible doctors. The Council on Physical Therapy of the American Medical Association exerted much effort in fostering education and research and to protect the profession and the public by critical evaluation of claims for apparatus.

World War II brought almost dramatic progress in the status of "physical medicine". Under this new definition physical medicine includes the employment of the physical and other effective properties of light, heat, cold, water, electricity, massage, manipulation, exercise, and mechanical devices for physical and occupational therapy in the diagnosis and treatment of diseases. The new term is much more comprehensive and adds dignity to this department of medicine. The impressive advancement in the status as well as in the overall employment of physical medicine was brought about by the redoubled efforts of medical leaders in the United States for the advancement in research and instruction, by efficient clinical usage and finally, by the realization of the vital importance of physical medicine as the keystone of physical rehabilitation. First came a large scale expansion of physical therapy departments in Army and Navy hospitals and other service centers, and an extensive training program of physicians and technicians in order

*Especially submitted for publication during the 15th Anniversary Year of the National Gastroenterological Association and the 15th Year of publication of the Review of Gastroenterology, 1948-1949.

to enable the proper functioning of the departments. There also came the creation of the Baruch Committee on Physical Medicine from the humanitarian instinct of a great American citizen; it brought about an extensive survey of the immediate needs of physical medicine in the United States and the donation of means to implement a program of adequate development. The nationwide publicity incidental to the Baruch gift in itself greatly stimulated interest by the medical profession and the public. Simultaneously further funds for research and study were granted by the National Foundation for Infantile Paralysis and the National Research Council.

As a result of all these events, the number of instruction and research centers and the number of adequately trained younger physicians embarking on a career in physical medicine increased very considerably. In the same proportion, the number of clinical and laboratory studies also rose. Postgraduate seminars are now being held regularly in various parts of the country. Instruction courses have been instituted by the United States Army, which placed the Physical Medicine Service in its hospitals at equal standing with medicine, surgery and psychiatry, and appointed a national board of civilian Consultants in Physical Medicine. The rejuvenated Veterans Administration employs at present over one hundred physicians, trained specialists in physical medicine and also working under the guidance of a board of Consultants. Finally, the Advisory Board of Medical Specialties of the American Medical Association approved the establishment of an American Board of Physical Medicine. This Board is now fully functioning and has conducted its first two qualifying examinations.

It is impossible within the scope of this article to go into the details of the progress and changes in the actual employment of various physical measures themselves. Electricity is still the most versatile and most efficient controllable therapeutic measure for medical as well as surgical purposes, for general practitioners and specialists alike.

Static electricity is now largely a matter of history; low frequency currents progressed from the simple galvanic-faradic coil for both treatment and electrodiagnosis to highly efficient electronic muscle stimulators, which allow definite control as to frequency, duration and energy peaks and to intricate methods of diagnosis by chronaxiemetry, electromyography etc. The modern uses of ion transfer of vasodilating drugs have brought about a new surge in the use of the galvanic current.

The method of inducing convulsions by means of an alternating current applied to the brain came about as an evolution from the more hazardous drug administration for shock therapy in mental disorders, especially in depressive states. High frequency electricity for both localized and general deep tissue heating in the form of shortwave diathermy is now perhaps the most extensively used form of physical treatment; unfortunately, short wave diathermy in the hands of the inexperienced becomes generally little more than a glorified heating pad, applied in a hit or miss manner, because of the crude method of estimation of

dosage and the lack of appreciation that treatment of different pathologic conditions requires clinical judgment and experience. There is no reason at all to discard the older long wave spark gap type of apparatus. During the past year a newer form of diathermy, deep tissue heating by microwaves (radar) was introduced. It appears to be in some respects safer and more convenient in application.

The employment of artificial ultraviolet irradiation has assumed much importance since its curative effect on rickets were reported. Air and food sterilization by predominantly bactericidal radiation has added newer progress.

Hypothermy, or the therapeutic use of cold, has been greatly stimulated by recent clinical research in military and industrial surgery. Hydrogymnastics or exercises and manipulation in therapeutic pools and tanks, together with the earlier employment of the whirlpool bath, or hydromassage, has brought hydrotherapy into more extensive use. Originally introduced for the redevelopment of muscles weakened by infantile paralysis and unable to work against gravity outside of the water, pool or tank exercise has been found useful in treatment of the sequelae of many traumatic conditions, of hemiplegia and chronic arthritis.

The institution of a nationwide program for rehabilitation of those disabled by war and war-connected industrial activity has brought about widespread attention to the importance of exercise and physical fitness. Instead of much of the cumbersome passive therapy apparatus of former years, the present tendency is to use early active exercise without any apparatus and later, either active exercise apparatus of simple construction or various devices of the curative workshop principle, aiming to restore function as well as the individual's habit of work.

The linking of medical rehabilitation with physical medicine has brought about concerted efforts for establishment of such departments in large civilian hospitals in conjunction with Rehabilitation Centers so as to put into actual practice the third phase of medicine—getting the worker back on the job—the first two being prevention and treatment. In conjunction with this new development, convalescent wards and new types of convalescent hospitals are being planned to do away with unnecessarily long hospital treatment and to give patients the benefit of immediate exercise and of other methods of physical and occupational therapy. In most institutions occupational therapy as a method of functional treatment has become organically correlated to the physical medicine department. Thus physical medicine has not only greatly advanced but also considerably broadened its horizon.

The constant progress of physical medicine and its new status of recognition offers increased opportunities of serving the medical profession and the public; it also entails new responsibilities. Physical medicine cannot be practiced apart from the general medicine and surgery; it must always be based on a definite diagnosis and the relative value of physical measures compared to other medical measures must always be taken into consideration; they serve as primary methods of treatment not as frequently as they do as valuable adjuncts to other forms of treatment. In the clinical practice of physical medicine it must be constantly

remembered that complicated apparatus does not form its most essential part. We do not treat a diagnosis with a piece of apparatus. Von Breemen stated many years ago: "the essence of physical therapy is the study and application of the correct dosage of stimulation with physical agents". Biophysics is the basis of physical medicine and constant clinical observation its chief guide, because the reaction of the individual is the unpredictable or variable factor. Hence the practice of physical medicine truly represents a blending of the science and art of healing and it should prove equally valuable in the hands of the general practitioner, the specialist in various branches and to the specialist in physical medicine now designated as a physiatrist.

THE EFFECT OF URINE EXTRACT FROM OÖPHORECTOMIZED DOGS ON GASTRIC SECRETION*†**

JERZY KAULBERSZ, PH.D., M.D.
THOMAS L. PATTERSON, PH.D., SC.D.
DAVID J. SANDWEISS, M.D.
and
HARRY C. SALTZSTEIN, M.D.
Detroit, Mich.

It was previously reported that urine extracts from dogs deprived of their ovaries did not inhibit gastric secretion as much as urine extracts obtained from normal animals[1, 2]. Because of the difference in the results of these two urine extracts it was deemed desirable to repeat the experiments. Additional urine was thus collected from oöphorectomized dogs and the extract was assayed on gastric pouch and fistula dogs.

METHOD OF STUDY

The same method as previously described[2] was used for extract preparations. The yield of the purified extract was comparable with that from normal dogs. The extracts were tested in double histamine experiments on four dogs with gastric fistula and five dogs with Heidenhain pouch. The extract was injected intravenously mostly in 2 mg. doses. Histamine diphosphate was administered subcutaneously in doses of 0.5 or 1.0 mg. 10 minutes after extract injection, and an identical dose was used in the control period. The interval between two periods was 3 hours. Total output of HCl for 70 minutes following histamine injection was regarded as a measure of gastric secretory response.

RESULTS

When urine extract was administered in the first period in 25 "double histamine" experiments an average stimulation of 9 per cent resulted; when given in the second period in 16 experiments an increase of 13 per cent was found as compared with the controls. In 2 experiments on 2 fistula dogs and 1 experiment on a pouch dog, considerable inhibition (72 per cent, 34 per cent and 26 per cent) of the secretion in response to 1 mg. histamine resulted when 4 mg. urine extract were administered in the first period. The remaining 38 experiments with 2 mg. doses of extracts were divided into uniform groups and subjected to statistical analysis, the results of which are given in Table I. It is seen from the table that extracts inhibited in a varying degree the effect of histamine on gastric secretion in three groups of experiments and enhanced it, also in a varying degree, in the

*From the Departments of Surgery and Physiology, Wayne University College of Medicine and the Research Division of Harper Hospital, Detroit, Michigan.

†Aided in part by grants from the Committee on Scientific Research of the American Medical Association and the Stewart Hamilton Research Fund, Detroit, Michigan.

**Especially submitted for publication during the 15th Anniversary Year of the National Gastroenterological Association and the 15th Year of publication of The Review of Gastroenterology, 1948-1949.

TABLE I

EFFECT OF URINE EXTRACT FROM OÖPHORECTOMIZED DOGS ON GASTRIC SECRETION IN DOUBLE HISTAMINE EXPERIMENTS

Series	Extract administered in	Type of Dog	No. of Dogs	No. of Experiments	Dose		Output of HCl (mE)				HCl output after Extract as % of Control	P*
					Extract mg.	Histamine mg.	Extract plus Histamine $\bar{X}_1$	S_1	Histamine only (Control) $\bar{X}_2$	S_2		
A	First Period	Fistula	3	9	2.0	1.0	9.3	2.8	6.9	1.2	134.5	0.41
		Pouch	2	5	2.0	1.0	1.70	0.55	1.80	0.02	94.5	0.71
		Pouch	3	8	2.0	0.5	0.85	0.40	1.44	0.47	59.0	0.005
B	Second Period	Fistula	4	8	2.0	1.0	8.0	4.7	6.7	3.5	119.0	0.49
		Pouch	2	3	2.0	1.0	1.2	0.4	1.9	0.9	63.3	0.21
		Pouch	3	5	2.0	0.5	1.25	0.55	1.11	0.49	112.5	0.67

$\bar{X}_1$ and $\bar{X}_2$ — mean; S_1 and S_2 — standard deviation.

*The difference $\bar{X} = \bar{X}_1 - \bar{X}_2$ is regarded significant when P is 0.05.

P values were estimated for $T = \bar{X}\frac{n(n-1)}{S_{X_2}}$ (Snedecor[3]).

other three groups. However, in only one group, comprising 8 experiments on pouch dogs, extract administered in the first period produced an average inhibition of 41 per cent which was highly significant statistically. It seems, therefore, that highly purified extracts obtained from oöphorectomized dogs contain so little urogastrone that its presence cannot be demonstrated uniformly with the technic which has been proven efficient with similarly prepared extracts from the urine of normal dogs.

Data presented in Table I also demonstrate that the administration of urine extract from oöphorectomized dogs did not produce any delayed effect on gastric secretion such as follows the administration of extracts from hypophysectomized dogs. This is evident from the fact that the response to histamine alone injected in the first period did not differ significantly from that after administration in the second period of the double histamine test, i.e. several hours after urine extract injection.

Discussion

The results of these experiments are in agreement with our previously reported studies and they seem to indicate that in the urine extracts from oöphorectomized dogs only very little urogastrone is present or perhaps none at all. Thus, the ovaries may have some relation to the urogastrone production. This relation may be direct or mediated by the hypophysis. The latter view seems to be justified by the fact that the pituitary gland, according to our investigation, exerts some influence on the formation, or excretion of urogastrone, in as much as urine of the hypophysectomized dogs does not inhibit gastric secretion as does normal urine extract.

Summary

Extracts obtained from urine of oöphorectomized dogs do not influence gastric secretion in response to histamine, as normal urine extracts do. The urogastrone in the urine may either be reduced in amount, or possibly be entirely absent.

REFERENCES

1. Kaulbersz, J., Patterson, T. L., Sandweiss, D. J. and Saltzstein, H. C.: Science. **102**:530, 1945.
2. Kaulbersz, J., Patterson, T. L., Sandweiss, D. J. and Saltzstein, H. C.: Am. J. Physiol. **150**:373, 1947.
3. Snedecor, George W.: Statistical Methods. Iowa State College Press, Ames, Iowa, 1946.

THE EFFECT OF URINE EXTRACT FROM THYROIDECTOMIZED DOGS ON GASTRIC SECRETION*†**

JERZY KAULBERSZ, PH.D., M.D.
THOMAS L. PATTERSON, PH.D., SC.D.
DAVID J. SANDWEISS, M.D.
and
HARRY C. SALTZSTEIN, M.D.
Detroit, Mich.

Earlier work revealed that urine extracts from dogs deprived of their ovaries do not inhibit gastric secretion as much as those of normal animals or perhaps even not at all[1, 2]. However, if in addition to the ovaries the thyroid gland is extirpated the inhibitory substance appears in the extracts in approximately normal quantities. Therefore, it was thought desirable to investigate the effect of urine extracts prepared from dogs from which only thyroid glands were removed.

TABLE I

EFFECT OF URINE EXTRACT FROM THYROIDECTOMIZED DOGS ON GASTRIC SECRETION IN DOUBLE HISTAMINE EXPERIMENTS
(Doses used: 5.0 mg. Extract and/or 0.5 mg. Histamine).

Extract Administration in	Type of Dog	No. of Dogs	No. of Experiments	Output of HCl (mE)				Per cent Inhibition after Extract	P*
				Extract plus Histamine		Histamine only (Control)			
				$\bar{X}_1$	S_1	$\bar{X}_2$	S_2		
1st	Fistula	1	4	4.4	2.8	10.5	5.7	58.2	0.0001
Period	Pouch	4	16	0.41	0.15	0.77	0.27	46.8	0.0001
2nd	Fistula	1	4	4.9	3.1	8.9	2.0	45.0	0.0076
Period	Pouch	2	12	0.44	0.17	0.63	0.20	30.1	0.0186

$\bar{X}_1$ and $\bar{X}_2$ — mean; S_1 and S_2 — standard deviation.
*The difference $\bar{X} = \bar{X}_1 - \bar{X}_2$ is regarded significant when P is 0.05.
P values were estimated for $T = \bar{X}\frac{n(n-1)}{Sx^2}$ (Snedecor[6]).

METHOD OF STUDY

Thyroidectomies were performed on six female dogs 1-3 weeks previous to the urine collection, special attention being given to the preservation of the parathyroids. In the first 3 weeks following the removal of the glands a decrease in the urine production was noted, as compared to the amount collected from the same animals preceding the thyroidectomy. The difference, however, did not exceed 20 per cent. During the next month this reduction was followed by an increase of urine excre-

*From the Departments of Surgery and Physiology, Wayne University College of Medicine and the Research Division of Harper Hospital, Detroit, Michigan.
†Aided in part by grants from the Committee on Scientific Research of the American Medical Association and the Stewart Hamilton Research Fund, Detroit, Michigan.
**Especially submitted for publication during the 15th Anniversary Year of the National Gastroenterological Association and the 15th Year of publication of The Review of Gastroenterology, 1948-1949.

tion, exceeding the normal by 15 per cent. Thereafter, the same quantities of urine were produced as before the operation.

The extracts were prepared and purified by the method of Gray et al.[3] and the final product was assayed on dogs with gastric fistula or Heidenhain pouches in "double histamine" experiments in the previously described manner[2], 2-5 mg. doses of the extract being used.

When urine extract from thyroidectomized dogs was injected in doses of from 2 to 5 mg. in the first period in 28 double histamine experiments, 26 inhibitions and 2 no differences were noted. The average inhibition of the total output of HCl amounted to 45 per cent. When administered in the second period in 19 double histamine experiments, 12 inhibitions, 1 stimulation and 6 no differences above ± 10 per cent were found. The average diminution of the total output of HCl equalled 50 per cent.

Experiments with 5 mg. doses of the extract, presented in Table I, were not uniform as indicated by very high values for standard deviations. Nevertheless, there was a uniform inhibition in all experiments with 5 mg. doses of extract which averaged, 45 per cent from all 36 experiments. Statistical analysis (Table I) demonstrated that the inhibition of that magnitude was unquestionably significant. With smaller doses (2 or 2½ mg.) of the extracts, but the same dose of histamine (0.5 mg.), results, which are not included in the table, were less uniform. When these doses of the extract were injected in the first period in two pouch dogs (3 experiments) 66 per cent inhibition resulted, in the third (2 experiments) 40 per cent and in the fourth (2 experiments) only 17 per cent, while in a fistula dog (1 experiment) 18 per cent stimulation occurred. When 2 mg. doses of the extract were introduced in the second period in 2 experiments on 2 pouch dogs, 1 stimulation and 1 no difference resulted, while in one experiment on a fistula dog 84 per cent inhibition was observed.

Discussion

In a previous communication[4] it was reported that when extract from urine of thyroidectomized dogs was injected in the first period of a double histamine experiment decrease in HCl output occurred in 21 out of 23 experiments and the average total output of free HCl was reduced 59.8 per cent. When the extract was administered in the second period in 14 experiments, 7 inhibitions, 1 stimulation, 6 no differences were observed with an average inhibition of 42 per cent. From the above observations and from the results of this study as well, it could have been concluded that the injection of the thyroid extract in the first period gives more pronounced inhibitory effect on gastric secretion in response to histamine than when injected in the second period. However, such conclusion does not seem to be justified since the differences between mean values for HCl output for the corresponding periods in both series of the present study (Table I) were obviously not significant.

Comparison of the above results with the effect of the extracts prepared from normal urine observed in our other experiments seems to suggest that urine of the

thyroidectomized dogs may yield extracts with more pronounced inhibition. However, the evidence obtained so far is not conclusive and further studies are necessary.

It is of interest that the average output of HCl in pouch dogs with histamine alone injected in the first period is not significantly different from that obtained when histamine was injected in the second period, i.e. several hours after urine extract was administered (Table I). We have seen that gastric response to histamine injected several hours after administration of the urine extract from hypophysectomized dogs was greatly diminished. This fact indicated that the nature of the inhibitory substance in these two extracts differs. Urine extracts from thyroidectomized dogs produced pronounced inhibition during the first 80 minutes after injection and, in this respect, were similar to the extracts from the urine of the normal dogs. Extracts prepared from urine of the hypophysectomized dogs produced no inhibition, rather a slight increase of secretion during the first 80 minutes but very strong inhibition after 5 or 8 hours, which therefore cannot be ascribed to normal urogastrone[5].

Summary

Thyroidectomized dogs' urine extracts produced a pronounced inhibition of gastric secretion after histamine administration. The general character of the response indicated that the inhibitory principle of these extracts in every respect is similar to the "urogastrone" of the normal urine.

References

1. Kaulbersz, J., Patterson, T. L., Sandweiss, D. J. and Saltzstein, H. C.: Science. **102**:530, 1945.
2. Kaulbersz, J., Patterson, T. L., Sandweiss, D. J. and Saltzstein, H. C.: Am. J. Physiol. **150**:373, 1947.
3. Gray, J. S., Wieczorowski, E., Wells, J. A. and Harris, S. C.: Endocrinology. **30**:129, 1942.
4. Kaulbersz, J., Patterson, T. L., Sandweiss, D. J. and Saltzstein, H. C.: Abstracts of Communications. XVIIth Intern. Physiol. Congress, Oxford, England, p. 372, 1947.
5. Kaulbersz, J., Patterson, T. L., Sandweiss, D. J. and Saltzstein, H. C.: The Effect of Urine Extract from Hypophysectomized Dogs on Gastric Secretion. To be published.
6. Snedecor, George W.: Statistical Methods. Iowa State College Press, Ames, Iowa, 1946.

For Anti-Flatulent Effects in Intestinal Putrefaction and Fermentation

NUCARPON®

Each tablet contains: Extract of Rhubarb, Senna, Precipitated Sulfur, Peppermint Oil and Fennel Oil, in a high activated willow charcoal base.
Action and uses: Mild laxative, adsorbent and carminative. For use in indigestion, hyperacidity, bloating and flatulence.
1 or 2 tablets daily ½ hour after meals. Bottles of 100.
STANDARD PHARMACEUTICAL CO., INC. 1123 Broadway, New York

EDITORIALS

THE SURGERY OF PORTAL OBSTRUCTION AND PORTAL HYPERTENSION

In civil practice, blood vessel surgery is, at present, largely concerned with the problem of the relief of portal obstruction and hypertension. Such obstruction may be of two types: that due to pathology inside the liver and that resulting from conditions without it.

Intrahepatic block is caused commonly by the Laennec type of hepatic cirrhosis. Extrahepatic block is frequently associated with splenic enlargements in which the lesion, in its later stages, is further extended by a secondary hepatic cirrhosis. Sometimes portal obstruction is due to congenitally acquired defect and/or pathology. Under any of such conditions, the block can be initiated and/or further intensified by thrombosis of the splenic vein. It is possible to distinguish between the intrahepatic and extrahepatic varieties of portal obstruction by liver functional tests. Blood vessel surgery is especially applicable to portal hypertension of cirrhotic origin. Relief is sought and accomplished by shunting the venous blood flow from the portal area to the general systemic venous blood circulation.

The idea of this procedure was first conceived by Eck of Pavlov's laboratory in Russia in 1872. He anastomosed the portal vein to the vena cava in a dog. Although not further attempted at that time in human beings, because of its hazard, the operation has, nevertheless, been perpetuated as a standard laboratory procedure known as Eck's fistula. The earliest successful attempts in humans were done by Rosenstein in Germany, and by Bogoraz in Russia.

Recently blood vessel surgery has been simplified by the development of a nonsuture method of blood vessel anastomosis by Blakemore and Lord[1] who make use of vitellium tubes for this purpose. Five such splenorenal anastomoses have been successfully done by Whipple and Blakemore[4] with simultaneous removal of the spleen and the left kidney. Five other end-to-side anastomoses between the portal vein and the vena cava have also been done by them. In comparison with this tube method, the suture method of vessel anastomosis, preferred by Blalock[2] is more difficult.

Linton and his group[3] prefer the following procedure: whenever possible they do an end-to-side splenorenal anastomosis after removal of the spleen and with preservation of the kidney. Other types of operation, which they have done, include anastomosis of the superior mesenteric vein to the inferior vena cava, and of the inferior mesenteric vein to the left ovarian vein; in these patients, the spleen is previously removed. Their experience indicates that direct union of the portal vein and the inferior vena cava is hazardous at times because of the extreme degree of vascularity in the region of the gastrohepatic ligament.

The hoped for effect of a successful operation of this kind lies in alleviation of the symptoms, in the prevention of serious hemorrhages from esophageal varices, and in the reduction of portal hypertension with consequent improvement in the liver function.

The successful development of this vascular surgery marks a distinct advance in the possibilities of modern surgery in general. Nevertheless, it will be of great interest to know what the late results of this method of treating portal hypertensions and obstructions will turn out to be, not only as regards the span of subsequent life when compared with other unoperated cases, but, also, as regards the subsequent extent and character of any morbidity due to the original illness. Some of this, at least, one expects will be present in an illness of this degree of pathological structural change in such vitally important organs. A. O. WILENSKY

REFERENCES

1. Blackmore, A. H. and Lord, J. W.: A Nonsuture Method of Blood Vessel Anastomosis. J.A.M.A. **127**:685, 1945.
2. Blalock, A.: The Use of Shunt or By-Pass Operations in the Treatment of Certain Circulatory Disorders; Including Portal Hypertension and Pulmonic Stenosis. Ann. Surg. **125**:129, 1947.
3. Linton, R. W., Hardy, I. B. and Volwiler, W.: Portacaval Shunts in the Treatment of Portal Hypertension. Surg. Gynec. & Obst. **87**:129, 1948.
4. Whipple, A. O.: The Problem of Portal Hypertension in Relation to the Hepatosplenopathies. Ann. Surg. **122**:449, 1945.

THE FIFTEENTH ANNIVERSARY OF THE REVIEW OF GASTROENTEROLOGY

This month marks fifteen years since the first issue of THE REVIEW OF GASTROENTEROLOGY appeared in 1934, as the pioneer journal in its field.

Founded by the present Editor, who has retained that position throughout the fifteen years, it became the official publication of the National Gastroenterological Association and has grown from a quarterly publication to a monthly publication devoted to gastroenterology, proctology and allied subjects. It succeeded and incorporated the American Journal of Gastroenterology, which was the *first* journal in this field to be published in the United States.

During this period two other publications appeared, but THE REVIEW OF GASTROENTEROLOGY is the *only* one which has consistently remained the official publication of any organization devoted exclusively to gastroenterology.

Throughout the years, the policy of the Editorial Board has been to publish papers of clinical value and material which the general practioner, the specialist in gastroenterology and those specializing in allied fields could apply in their daily practice. From time to time, papers on various research matters have appeared and will continue to appear in its pages, but fundamentally, the purposes of THE REVIEW OF GASTROENTEROLOGY are to bring to physicians information which they can use and apply in actual practice.

During the coming years it is anticipated that several new features will be added to the publication which will enhance its value to the members of the National Gastroenterological Association, subscribers and medical profession generally.

The Editor wishes to personally thank each and every one of the members of the staff who have so ably served these fifteen years, the authors who have so generously contributed their time and material for publication in THE REVIEW OF GASTROENTEROLOGY, the officers, members, Executive Board of the National

Gastroenterological Association for their confidence and trust in him, the members of the staff of the headquarters office who are responsible for the production of the journal, our advertising manager, Mr. Steven K. Herlitz for his untiring efforts in our behalf, and last but not least—all those advertisers who have constantly throughout the years, supported the journal in its efforts to bring a much needed service to the members of our profession.

SAMUEL WEISS

Have a Coke

Turn to Refreshment

Drink Coca-Cola

CHAPTER ACTIVITIES

Boston Chapter

A meeting of the Boston Chapter of the National Gastroenterological Association was held at the City Hospital in Boston on Friday, 4 February 1949.

The speaker at the meeting was Dr. Richard Schatzki of Boston.

Over 100 members and guests attended the luncheon and several new applications for membership have been received from those present.

Los Angeles Chapter

A meeting of the Los Angeles Chapter of the National Gastroenterological Association was held on 4 January 1949 at the Queen of Angels Hospital in Los Angeles, California.

The guest speaker was Dr. Howard B. Carroll, Associate Professor of Medicine, Northwestern University of Chicago who spoke on "Diverticula of the Small Bowel".

The paper was discussed by Dr. William Brown, Roentgenologist at Hollywood Presbyterian Hospital of Los Angeles, who amplified his discussion with a movie film of x-ray pictures.

Members of the Los Angeles Chapter as well as their guests attended the meeting.

Rhode Island Chapter

A meeting of the Rhode Island Chapter of the National Gastroenterological Association was held in Providence, R. I., Wednesday evening, 9 March 1949.

Dr. Halsey B. Loder, President of the Boston Chapter of the Association was the speaker of the evening.

New Jersey Chapter

A meeting of the New Jersey Chapter held at the Academy of Medicine in Newark on Monday evening, 7 February 1949 was well attended.

The program of the evening featured a scientific session.

New York Chapter

The next regularly scheduled meeting of the New York Chapter of the National Gastroenterological Association will be held on Monday evening, 14 March 1949 at the New York Academy of Medicine.

The speakers will be: Dr. Clarence C. Fuller, Associate Clinical Professor of Postgraduate Medical School of New York University, "Newer Concepts in the Treatment of Ulcerative Colitis"; Dr. Nathan Lane, "Lysozyme Activity in Chronic Ulcerative Colitis" and Dr. Linn J. Boyd, Director of Department of Medicine, New York Medical College, Dr. George B. Jerzy Glass, Assistant Clinical Professor of Medicine, New York Medical College, "New Clinical and Physiological Studies on the Secretion of Mucin in the Human Stomach".

Members of the Chapter, the Association, their staff and guests are cordially invited to attend.

NEWS NOTES

President of the Royal College of Surgeons to Speak at Convention

In a letter to Dr. William Reid Morrison, President and Chairman of the Program Committee of the National Gastroenterological Association, Sir Alfred Webb Johnson, President of the Royal College of Surgeons, advised that he had reconsidered his decision not to come to the United States for our Convention, and that he is glad to accept our invitation to be present and speak at one of the scientific sessions.

Dr. Morrison also announces that Dr. Paul B. Magnuson, Medical Director of the Veterans Administration, has accepted an invitation to be a speaker at the Annual Convention Banquet to be held on Tuesday evening, 25 October 1949 at the Hotel Somerset in Boston, Mass. An honored guest at the Banquet will be Mr. James Rand, Jr. chairman of the Board of Remington Rand, Inc.

The Program Committee announces that valuable gifts have been received for distribution to those attending the Convention Banquet.

Reservations for Hotel accommodations can be made through the National Gastroenterological Association headquarters, 1819 Broadway, New York 23, N. Y. Members will receive reservation cards along with the copy of Monthly Bulletin to be mailed during the month of March.

The Program for the Convention will be published in the September 1949 issue of The Review of Gastroenterology and when completed, copies will be available upon request.

Annual Meeting of the American College of Allergists

The Annual Meeting of the American College of Allergists will be held in Chicago, Ill. 14-17 April 1949.

Members and non-members of the College are invited to attend and all are required to register and receive a badge. There will be no charge for registration.

The scientific sessions and exhibits will be held at the Palmer House in Chicago and the papers will range from the most practical application of diagnosis and therapy in allergic diseases to investigate fields of great importance.

In Memoriam

We record with profound sorrow the passing of Dr. B. J. Bixby of Buffalo, N. Y. and Dr. Abraham O. Wilensky of New York, N. Y.

Both Dr. Bixby and Dr. Wilensky were for many years members of the Editorial Council of The Review of Gastroenterology and in previous years members of the National Gastroenterological Association.

We extend to the families of the deceased our deepest sympathies.

ABSTRACTS

Esophagus

RESECTION OF THORACIC ESOPHAGUS FOR CARCINOMA LOCATED ABOVE ARCH OF AORTA: CERVICAL ESOPHAGOGASTROSTOMY. John H. Garlock. Surgery. **24**:1-8, (July), 1948.

The least frequent site for cancer of the esophagus is that portion located above the superior border of the aortic arch, the superior mediastinum. This portion is approached (surgically) with difficulty. Tumors in this location are frequently locally inoperable when first seen by the surgeon.

Garlock reports a case in a woman aged 46 years, upon whom he operated January 3, 1947, at Mount Sinai Hospital in New York. The operation took four and one-half hours, during which she received 1,500 cc. of whole blood.

The patient died suddenly the next morning. Postmortem examination did not reveal any cause of death. Perhaps, death was due to "profound physiologic disturbances, possibly caused by vagal stimulation".

Hyman I. Goldstein

Stomach

TUBERCULOSIS OF THE STOMACH AND DUODENUM. Herman W. Ostrum and William Serber. Am. J. Roentgenol. **60**:315, (Sept.), 1948.

Two cases of tuberculosis of the stomach and one of the duodenum are described. In all three cases the lungs showed no active pulmonary tuberculosis. One patient had a peripheral tuberculous adenitis for years, and in all three cases abdominal lymph node involvement was a very prominent feature. All three patients developed perforations or fistulous tracts at the site of their lesions. From the roentgenological standpoint there are no pathognomonic findings. The ulcerative and infiltrative lesions can easily be confused with benign ulcer or carcinoma. A combination of both types of lesions, as well as extensive mucosal nodularity, might be suggestive. The most significant findings that can be demonstrated roentgenologically are simultaneous involvement of the stomach and duodenum, the presence of fistula or sinuses, and signs of external pressure by enlarged lymph nodes.

Franz J. Lust

THE GASTROSCOPIC PICTURE IN POSTIRRADIATION GASTRITIS. Eddy D. Palmer. Am. J. Roentgenol. **60**:360, (Sept.), 1948.

Gastroscopic studies in twelve patients who had developed postirradiation gastritis following intensive radiation treatment for malignant disease showed remarkably constant and characteristic gastric changes. The picture included marked edema with tubular deformity and fixation of the antrum, similar fixed patulousness of the pylorus, and clean deep chronic ulcers which healed without contracture. Following subtotal gastrectomy with posterior gastroenterostomy, the picture was that of normal postoperative stomach. Pathologic and roentgenographic studies in general corroborated the gastroscopic findings. A new gastroscopic entity is presented, but, because the diagnosis of postirradiation gastritis should be obvious from the history, the importance of endoscopy lies in the evaluation of the severity of the radiation damage.

Franz J. Lust

TRANSTHORACIC GASTRECTOMY. Giles A. Coors. Memphis M. J. **13**:176, (Oct.), 1948.

The author reminds us that up until about ten years ago surgeons generally were of the opinion that malignancies of the cardiac end of the stomach, involving the esophagus, were practically always inoperable. Previously there existed a dread of invading the pleural cavity due to the fact that the outcome was usually fatal. Because of a better understanding of the physiology of the open thorax and the administration of a positive pressure anesthetic with an indwelling tracheal tube, it is now possible to open a pleural cavity and maintain respiration and life with impunity.

He touches lightly on the usual symptoms of neoplasms in the region of the esophagus and cardia and outlines the usual diagnostic procedures of roentgenology and esophagoscopy. Preoperative administration of sulfa, Vitamins B-complex and C, high carbohydrate and high protein diet and the administration of large quantities of blood is stressed.

The author appears to favor the Garlock method of combined abdominathoracic approach which has the advantage of allowing a decision as to metastasis in the liver, peritoneum, lymph nodes or adjacent unresectable tissues or organs. In the author's opinion, involvement of the spleen or tail of the pancreas may be readily resected with the original growth and he cites reports of the removal of a portion of the left lobe of the liver.

It is easily possible to resect the entire stomach, spleen and tail of the pancreas, and ligation of the arterial blood supply to the stomach as it emerges from the celiac axis is facilitated. The duodenum and remaining abdominal pouch of the stomach may be readily elevated into the thoracic

vertebrae and the anastomosis of the esophagus and stomach pouch can be carried out under direct vision without tension. Posterior sutures can be placed in the esophagus before the esophagus is cut above the new growth. Silk sutures are used throughout. A Levin tube is passed down through the anastomosis and into the stomach pouch in order to allow for syphon drainage and the administration of fluids without the process of swallowing.

Postoperative care consists of:

(1) Aspiration of chest fluids, if present, through an indwelling under water catheter.
(2) Routine use of oxygen for at least 24 hours after the operation.
(3) Removal of chest drainage tube about 72 hours after operation if no fluid is present.
(4) Daily administration, intravenously, of glucose, salt, amino acids and blood.
(5) Feeding on the 1st to the 6th day, starting with 1 oz. of water every hour and adding solids as tolerated.
(6) Penicillin in large amounts.

Dr. Coors quotes an immediate operative mortality of about 17 per cent and mentions the fact that we are dealing with a condition that previously gave a 100 per cent mortality with nonsurgical treatment and contrasts the prolongation of a useful life for a very variable period of time, although we do not expect, nor do we get, a high percentage of 5 year cures. He presented a patient who was operated upon approximately one year ago, a portion of the esophagus and the cardiac portion of the stomach having been resected. This patient had regained his normal weight and was working every day, although an x-ray examination completed just prior to the presentation of his case revealed a suspicion of a local recurrence. JOHN E. COX

SURGICAL TREATMENT OF GASTRIC, DUODENAL AND GASTROJEJUNAL ULCER, INCLUDING THE PRESENT STATUS OF VAGOTOMY. Ralph Colp. Bull. New York Acad. Med. **24**:755, (Dec.), 1948.

Vagotomy as a sole procedure has been abandoned in the treatment of unobstructed duodenal ulcer as a result of Colp's experiences in a series of twenty-one cases, because seven of them required further surgery, two for recurrent duodenal ulcer, and five for gastric dilatation and atony. The completeness of the division of the vagi as evidenced by the insulin test bears no relationship to the clinical results. The addition of gastroenterostomy to vagotomy seems to have eliminated the undesirable effects of gastric atony in 26 cases of duodenal ulcer in which it was performed. Whether the incidence of gastrojejunal ulceration will be lessened by the combination of vagotomy and gastroenterostomy, as compared to gastroenterostomy alone, only long range follow-up studies will determine. Gastroenterostomy combined with bilateral infradiaphragmatic vagotomy is the preferred procedure in cases of duodenal ulcer unsuitable for subtotal gastrectomy.

For Colp the subtotal gastrectomy still remains the operation of choice in duodenal ulcer. It has been combined with infradiaphragmatic vagotomy in a series of patients whose preoperative acidity was high, and who had a tendency to bleed. There has been no increase in the operative mortality and a slight increase in the postoperative morbidity attributable to the added vagotomy. Whether the incidence of recurrent gastrojejunal ulceration will be diminished remains a subject for further study.

The immediate results of vagotomy in the treatment of gastrojejunal ulceration following gastroenterostomy and subtotal gastrectomy have been excellent. Subsequent follow-up has revealed recurrent ulceration in some cases. In patients considered to be good operative risks, a subtotal gastrectomy with infradiaphragmatic vagotomy is preferable to vagotomy alone for gastrojejunal ulceration following gastroenterostomy. In gastrojejunal ulceration following subtotal gastrectomy, wherever possible resection of the ulcer and further gastric resection combined with infradiaphragmatic vagotomy would seem preferable to the severance of the vagus nerves alone.

Vagotomy is not indicated in the treatment of gastric ulcer. FRANZ J. LUST

INTESTINES

MUCOSAL STUDIES IN COLITIS DUE TO PARASITES. Julian Arendt and Jack Coheen. Am. J. Roentgenol. **59**:865, (June), 1948.

The authors studied 32 cases of parasite infections of the colon. In a high percentage of these cases, mucosal changes, such as spider-like widening and derangements of the folds, were found in typical localizations, particularly in the cecum pole, ascending colon and sigmoid. Increased spasticity was observed in these areas, in combination with mucosal changes sometimes taking the form of the previously described cone-shaped cecum pole. Not only severe but also milder types of Endameba hystolytica infections and one case each of Diendameba fragilis and of Monilia invasion showed deviations from the normal.

Changes in the cecal area and lower ascending colon combined with deviations from the normal in the sigmoid are strongly suggestive of protozoan infection. Continuous involvement of the colon

ascending from the rectum and sigmoid suggests ulcerative colitis. The character of the various ulcerations provides another point of differentiation. The demonstration of amebic ulcerations in the cecum pole is barely possible. FRANZ J. LUST

PRIMARY TUMORS OF THE JEJUNUM AND ILEUM. J. H. Eckel. Surgery. **23**:467-475, (March), 1948.

Primary tumors of the jejunum and ileum are quite rare.

Eckel reports twelve cases with malignant tumors—8 men and 4 women. The youngest was a man, 34 years old, with multiple lymphosarcoma of the jejunum. The duration of symptoms being nearly 13 months. Loss of weight was a prominent symptom, 9 of the 12 cases, lost considerable weight, the average loss being over 18 pounds. Anemia was present in 8 patients. Fatigue and weakness was recorded in all the cases. Six of the 12 patients had tarry stools (melena). In 7 cases a palpable abdominal mass was present. The author reports a total of 19 cases of tumor of the jejunum and ileum, 12 were malignant lesions, 7 patients had benign tumors, including, leiomyoma, lipoma, fibroma, and polyp.

A history of intermittent intestinal obstruction and melena and the presence of occult blood in the stool are of great diagnostic significance. The small intestinal barium series will establish the diagnosis in a high percentage of cases. HYMAN I. GOLDSTEIN

EXTRINSIC DEFORMITIES OF THE COLON. Robert C. Pendergrass. Radiology. **51**:320, (Sept.), 1948.

Extrinsic deformities of the colon may be roughly grouped as follows:

1) Deformities from enlarged viscera, including tumors of these viscera.

2) Deformities from inflammatory processes, adhesions and endometriosis.

3) Deformities from retroperitoneal tumors, mesenteric tumors, and omental tumors.

4) Deformities from tumors of the colonic wall not invading the mucosa.

5) Deformity from intraabdominal and inguinal hernia.

Instructive roentgenograms accompany this article. There are cases of: depression of the hepatic flexure by carcinoma of the kidney; aspect of colon before and after drainage of a perirenal abscess; appendiceal abscess; leiomyosarcoma of the colonic wall; ileocecal tuberculosis; internal hernia simulating displacement by intraabdominal masses. FRANZ J. LUST

BARIUM SULFATE IN SALINE SUSPENSION.—EXAMINATION OF THE COLON IN THE PRESENCE OF PARTIAL OBSTRUCTION. George M. Wyatt. Radiology. **51**:326, (Sept.), 1948.

There is a small group of patients with symptoms of unexplained rectal bleeding or abdominal tumor who present an unusually difficult diagnostic problem to the roentgenologist. These patients fall into two categories:

1) The patient who cannot retain an enema because of a relaxed or damaged anal sphincter or perineum.

2) Patients who do not have clinical obstruction or dilatation of the intestine but who present complete obstruction to the retrograde passage of a barium enema. It is with this group of patients that this paper is primarily concerned. Many of these patients have diverticulitis, and a small percentage also have a rectal bleeding due to diverticulitis.

Oral adminstration of barium in the presence of obstruction of the lower bowel is considered dangerous because of the probability of dehydration and impactation. Even normal patients often have difficulty in expelling the barium. One logical method of preventing dehydration of the barium is to administer it with a saline cathartic which, by its nature, maintains and increases liquefaction of the contents of the colon. The author's method is to have the patient hospitalized. Four ounces of barium is mixed with eight oz. of magnesium citratis. This mixture is given orally early in the morning and the patient is allowed water ad lib. Another 8 oz. of magnesium citrate, without additional barium is given about an hour and a half later, and fluoroscopy is then done at intervals starting about two hours following the administration of the barium. The speed of the passage of the barium-saline mixture varies markedly with the degree of obstruction and the age and physical activity of the patient. Excretion is usually almost complete at the end of eighteen hours or earlier. Such patients must obviously be kept under roentgenological observation until the barium is excreted and should be kept in the hospital for facilitation of such observation.

Excellent roentgenograms demonstrating cases of neoplasms and diverticulitis illustrate the author's method. FRANZ J. LUST

Pathology and Laboratory Research

PREPYLORIC SPASM SIMULATING GASTRIC MALIGNANCY. Allan L. Cohn and R. L. Gold. Gastroenterology. **10**:782-791, (May), 1948.

Persistent spasm of prepyloric or antral region of the stomach occasionally causes difficulty in diagnosis simulating malignancy. Eight cases are reported in which prepyloric spasm simulated antral malignancy. Thorough studies are required to make a correct differential diagnosis.

When a malignant lesion cannot definitely be excluded by all diagnostic aids, exploratory operation is indicated, gastroscopy, roentgenologic examination, antispasmodic remedies, may aid in diagnosis. Localized gastritis, benign pyloric hypertrophy, small ulcer with some induration, and a benign or malignant intramural lesion, may be a factor. If in doubt, exploratory operation is justified, to avoid overlooking early malignancy. Hyman I. Goldstein

---

TRUE PERNICIOUS ANEMIA WITHOUT ACHLORHYDRIA. A. Murphy. M. J. Australia. **1**:521-530, (Apr. 24), 1948.

Murphy reviews the literature on pernicious anemia particularly concerning achlorhydria.

He seems to prove satisfactorily that pernicious anemia does occur in association with free hydrochloric acid in the gastric secretion, that achlorhydria is not essential to the development of true Combe-Addison (idiopathic) progressive pernicious anemia. The author discusses Morrison's theory of dissociated dual function of the (acid secreting) oxyntic cells. These oxyntic cells are of normal appearance in achlorhydria. They disappear in pernicious anemia with loss of intrinsic factor and acid. Where acid is present, these cells may be expected to be "normally" present too.
Hyman I. Goldstein

DEPOSITION OF PROTEIN IN THE LIVER FOLLOWING INTRAVENOUS INJECTION OF AN AMINO ACID MIXTURE (HYDROLYZED PROTEIN) AND GLUCOSE. C. A. Ross and R. Elman. Science. **108**:441-443, (Oct. 22), 1948.

Chemical and histologic evidence was previously reported by Elman and associates that protein is deposited in the cytoplasm of protein-depleted hepatic cells by the administration of a high protein diet by mouth. The same is true when all food is administered intravenously.

Their experiments were carried out on adult dogs. They conclude that intravenous injection of an amino acid mixture (hydrolyzed protein) leads to a deposition of tissue protein in the liver.
Hyman I. Goldstein

THE USE OF RUTIN IN HEREDITARY HEMORRHAGIC TELANGIECTASIA. E. P. Cope and R. W. Grover, Jr. Investigative Determatology. **10**:39, (Feb.), 1948.

Cope and Grove report a case of a man, 27 years old, who, at 19 years began to have several telangiectases, between 1938 and 1941, and at 25 years he began to suffer from epistaxis 2 or 3 times a day. The personal and family history were not significant. There were no other instances of telangiectases or bleeding in any members of the family.

Cope and Grover report improvement in their patient following the use of rutin. The lesions were treated by electrolysis. Hyman I. Goldstein

---

EFFECT OF GALACTOSE ON THE UTILIZATION OF FAT. C. P. Richter. Science. **108**:449-450, (Oct. 22), 1948.

Schantz, Elvehjem, and Hart have shown that fat plays an important part in the utilization of galactose. Similar reports were made by Geyer, Boutwell, Elvehjem, and Hart. In these present experiments (on domestic Norway rats), the authors have shown that galactose plays an important part in the utilization of fat. They suggest, that consideration might be given to the addition of lactose, galactose, or skim milk powder to common fats and oils, for the diet of man.
Hyman I. Goldstein

BOOK REVIEWS

SYNOPSIS OF PEDIATRICS. John Zahorsky, A.B., M.D., F.A.C.P., Professor of Pediatrics, St. Louis University School of Medicine; Assisted by, T. T. Zahorsky, B.S., M.D., Senior Instructor in Pediatrics, St. Louis University School of Medicine. 158 Illustrations, Fifth Edition, 449 Pages, C. V. Mosby Co., St. Louis, 1948. Price $5.50.

In this fifth edition the authors have been careful to select facts which will be useful to the practitioner of medicine and which also will give the medical student an insight into pediatric medicine.

Many new drugs useful in pediatric practice have been added to the volume.

There are sixty-two chapters and an appendix. The latter deals with drugs and their dosage.

The text is clear, comprehensive, although the type is small it is easily read.

The illustrations including x-rays and colored plates help to assimilate the description given in the text.

As an example, the reader will find colored plates depicting scarlatinal sore throat and tongue (opposite page 178); another colored plate opposite page 184 illustrating Koplik's spots. A study of these two will immediately call to the attention of the student the variation between these two diseases.

Although the reviewer is not a pediatrician he occasionally sees a young child who is referred to him by the pediatrician or general practitioner.

In eliciting the history from the mother it is surprising to learn that the child has had difficulty moving its bowels or at times streaks of blood were present on the feces or on the toilet paper. On page 309 two short paragraphs give suggestions as to possible causes and treatment, which, when carefully followed will undoubtedly relieve the little patient. The use of soap enemas even in adults tend to increase the irritation of the mucous membrane and may even cause sloughing and bleeding.

The reviewer thoroughly enjoyed reading this volume and recommends it heartily.

GENERAL ENDOCRINOLOGY. C. Donnell Turner, Ph.D., Associate Professor of Zoology at Northwestern University. 1st edition. 604 pages with 164 figures. W. B. Saunders Company, Philadelphia and London, 1948. Price $6.75.

This timely volume on endocrinology written by an authority and gotten up in a format which is easily read and more easily comprehended should receive favorable comment from the medical profession.

In looking over the contents the reviewer is impressed by the wealth of material which this volume presents. For example, the chapters on the pancreas and gastrointestinal tract contain the newer knowledge regarding their function, etc.

On page 190 the reader will find interesting discussions on Principles from the duodenal mucosa; page 197, Cholecystitis and on page 192 Antiulcer hormones are discussed.

The bibliography at the end of the chapter is voluminous and up-to-date. The illustrations are clear and explicit.

CANCER MANUAL, STANDARDS FOR THE DIAGNOSIS AND TREATMENT OF CANCER. Cancer Foundation of the Iowa State Medical Society. 160 pages. 2nd edition, 1948.

This cancer manual deals with the fundamentals of cancer diagnosis. Both the general practitioner and the specialist will find it useful and instructive.

It covers cancer diagnosis thoroughly both as to early and late signs and the appropriate treatment for the case under consideration.

The committee is to be commended and the Iowa State Medical Society is to be congratulated for spending the members' money on such a useful and well timed manual. It is rather regrettable that other medical societies are not using the monies to good advantage, for the education and enlightenment of thousands of their members.

A PRACTICAL MANUAL OF DISEASES OF THE CHEST. Maurice Davidson, M.A., M.D., F.R.C.P. Physician to the Brompton Hospital for Consumption and Diseases of the Chest. Consulting Physician to the Miller General and Western Ophthalmic Hospitals. Geoffrey Cumberlege. Third Edition, 670 pages. Oxford University Press, London, N. Y., Toronto, 1948. Price $16.50.

This edition is an improvement over the previous editions. The volume is deserving of a prominent place on the desk of every clinican, phthisiologist, thoracic surgeon, and should be made available to all medical students, internes, and residents of all hospitals and medical schools, and particularly, should be carefully perused by the members of the staffs of hospitals for chest diseases.

A number of excellent books on "Diseases of the Chest" and on "Tuberculosis", have appeared in recent years. This textbook by Dr. Davidson deserves to be ranked among the best. An instructive section on elementary anatomy and physiology, and a chapter on radiology of the chest—make interesting reading.

The experienced author discusses bronchiectasis, foreign bodies, asthma, pleurisy, pulmonary edema and infarction, pneumonia, chronic pulmonary catarrh, the pneumoconioses, pulmonary tuberculosis (151 pages), empyema, abscess and gangrene of the lung, malignant new growths lymphadenoma, cysts of the lung and pleura, and sarcoidosis—(Besnier-Boeck-Schaumann Disease).

The illustrations—tomograms and radiograms—are excellent. The publishers are to be complimented for a fine book, high quality paper and good printing. This textbook will be widely read and appreciated for sometime to come.

PREOPERATIVE AND POSTOPERATIVE CARE OF SURGICAL PATIENTS. Hugh C. Ilgenfritz, A.B., M.D., F.A.C.S., Formerly Assistant Professor of Surgery, Louisiana State University School of Medicine, and Visiting Surgeon, Charity Hospital of Louisiana at New Orleans, foreword by Urban Maes, M.D., D.Sc., F.A.C.S., New Orleans. 898 pages, illustrated, C. V. Mosby Company, St. Louis, Mo., 1948. Price $10.00.

This volume gives systematic helpful information on the proper preparation and postoperative management of the surgical patient. The physiologic basis, and reasons for each of the various therapeutic measures advocated by the author are clearly and understandably discussed.

The information given is up-to-date, and includes many of the newer methods now being used in the leading surgical clinics.

Fluid and electrolyte balance is a subject of great importance and is informatively presented by the author in Chapter 2 (28 pages). Reference is made to the work of Coller and his associates, Ravdin and Johnston, Tocantins, and Maddock and Coller.

Metabolism and Nutrition—including protein deficiency and protein replacement are discussed in Chapter 3 (28 pages). Sedative medication and choice of anesthetic agent, are presented briefly in Chapter 4.

Shock, transfusion, vitamin deficiency states, chemotherapeutic and antibiotic drugs, postoperative complications—shock, septicemia, atelectasis or massive collapse of the lung, thrombophlebitis, pulmonary embolism—are adequately discussed. Other subjects receiving attention are: intestinal obstruction and peritonitis, wound-care, burns, thoracic surgery, gastrointestinal surgery, gynecologic surgery, dietary instruction (801-802), oxygen administration, and preparation for x-ray studies.

This book is recommended for the surgical residents and internes and for all general and special surgeons, interested in better preoperative and postoperative care of surgical patients.

PROCTOLOGY FOR THE GENERAL PRACTITIONER. Frederick C. Smith, M.D., M. Sc., F.A.P.S., F.I.C.S., Proctologist to Physicians' and Surgeons' Hospital and Kensington Hospital, Philadelphia, Fellow Philadelphia College of Physicians, etc. Fourth Edition, 466 pages. F. A. Davis Company, Philadelphia, 1948. Price $6.00.

In this new fourth edition of a practical text book on proctology for the general practitioner, the experienced author, has brought the work up-to-date by including information on the sulfa drugs, antibiotics and antihistaminics in relation to proctologic conditions.

The author informatively discusses anorectal symptomatology, embryology and anatomy, malformations of the anus and rectum, examination and diagnosis, preoperative and postoperative treatment, and anesthesia—local, general, and regional. Among the conditions briefly, but adequately covered by the author are: anal ulcer, cryptitis, and papillitis, hemorrhoids, prolapse and procidentia, pruritus ani, abscesses and fistula, pectenosis and stricture of the rectum colitis, anorectal tuberculosis, venereal diseases of the anus and rectum and parasites.

The closing chapters are concerned with constipation, diarrhea and fecal impaction, benign and malignant neoplasms—and surgery of the colon. Chapter 22 covers some additional therapeutic measures—relief pain, irrigations, suppositories, dressings, ultraviolet, nutrient enemas, etc.

This readable and practical book on proctology is recommended for internes, residents, and general practitioners and may well be used as a condensed text by junior and senior medical students in our medical schools.

CLINICAL UROLOGY. Lowrain E. McCoca, M.D., Clinical Professor of Proctology, Temple University. 503 pages, 263 illustrations, 7 in color. Second Edition. F. A. Davis Company, Philadelphia. 1948. Price $6.50.

The author of this book on clinical urology has had wide experience in this specialty at Temple University, and at the Philadelphia General Hospital where he is attending urologist and in a busy private practice.

This book has been favorably received. The author ably and satisfactorily covers most of the essentials of diagnosis and treatment. Ample space is allocated (91 pages) to "The Study of the Patient". Most of the more common diseases are adequately, if briefly, discussed by the author.

Diseases of the penis and urethra, of the scrotum and the prostate are covered in 3 chapters of 139 pages. Diseases of the bladder, ureters, and of the kidneys are interestingly and instructively presented.

There are chapters on impotence and sterility, urology in the female, and urology in children.

The illustrations are good and are quite helpful to the reader.

There is an excellent index of 58 pages. This book is recommended to all physicians, residents and internes interested in urology.

DETAILED ATLAS OF THE HEAD AND NECK. Raymond C. Truex, M.D., Ph.D., Associate Professor of Anatomy, College of Physicians and Surgeons, Columbia University and Carl E. Kellner, Artist, Department of Anatomy, College of Physicians and Surgeons, Columbia University. 162 pages. Oxford University Press, New York, 1948. $15.00.

This atlas of the head and neck with its many beautiful and very instructive colored and black and white illustrations, is the finest atlas of its kind that has appeared in recent years.

The authors and publishers are deserving of the plaudits and many expressions of praise that will be given them for this beautiful volume.

Every medical library, every medical school, and every surgeon interested in the head and neck, and all instructors of head and neck anatomy and surgery, should have a copy of this atlas.

ONLY BELLERGAL PROVIDES ALL THREE

1. **SYMPATHETIC INHIBITION with ergotamine tartrate.**
2. **PARASYMPATHETIC INHIBITION with Bellafoline.**
3. **CENTRAL SEDATION with phenobarbital.**

SANDOZ

Originality • Elegance • Perfection

FOR FUNCTIONAL DISORDERS

Patients with psychosomatic disorders **suffer somatic distress just as much as those with organic disease.**

For these patients Bellergal provides an effective combination of drugs acting on both divisions of the autonomic nervous system as well as on the central nervous system.

Use Bellergal in the treatment of gastrointestinal neuroses and other functional disorders.

Bellergal

SANDOZ PHARMACEUTICALS
Division of **SANDOZ CHEMICAL WORKS, INC.**
60-72 CHARLTON STREET, NEW YORK 14, N. Y.

EDER - CHAMBERLIN
GASTROSCOPE
MODEL NO. 400

The new Eder Gastroscope with the adjustable tip angulated from the ocular end is a remarkable advancement in gastroscopy. The well known clarity and fine definition of the Eder Flexible and Eder Flexi-Rigid Gastroscopes are combined in this new Model 400 and further improved by the coated lens system used now on all our instruments.

The outstanding feature can easily be recognized from the illustration. The possibility of bending the tip reduces the so-called "blind areas" considerably, especially against the posterior wall where it is possible now to move the objective window away giving a perfect view of this lesion. Many other areas can be visualized and brought closer to the eye of the examining doctor. Using both angles of 30 degrees up and 30 degrees down including angle of vision of 40 degrees of the optical system it is possible to achieve an angle of visualization of 100 degrees.

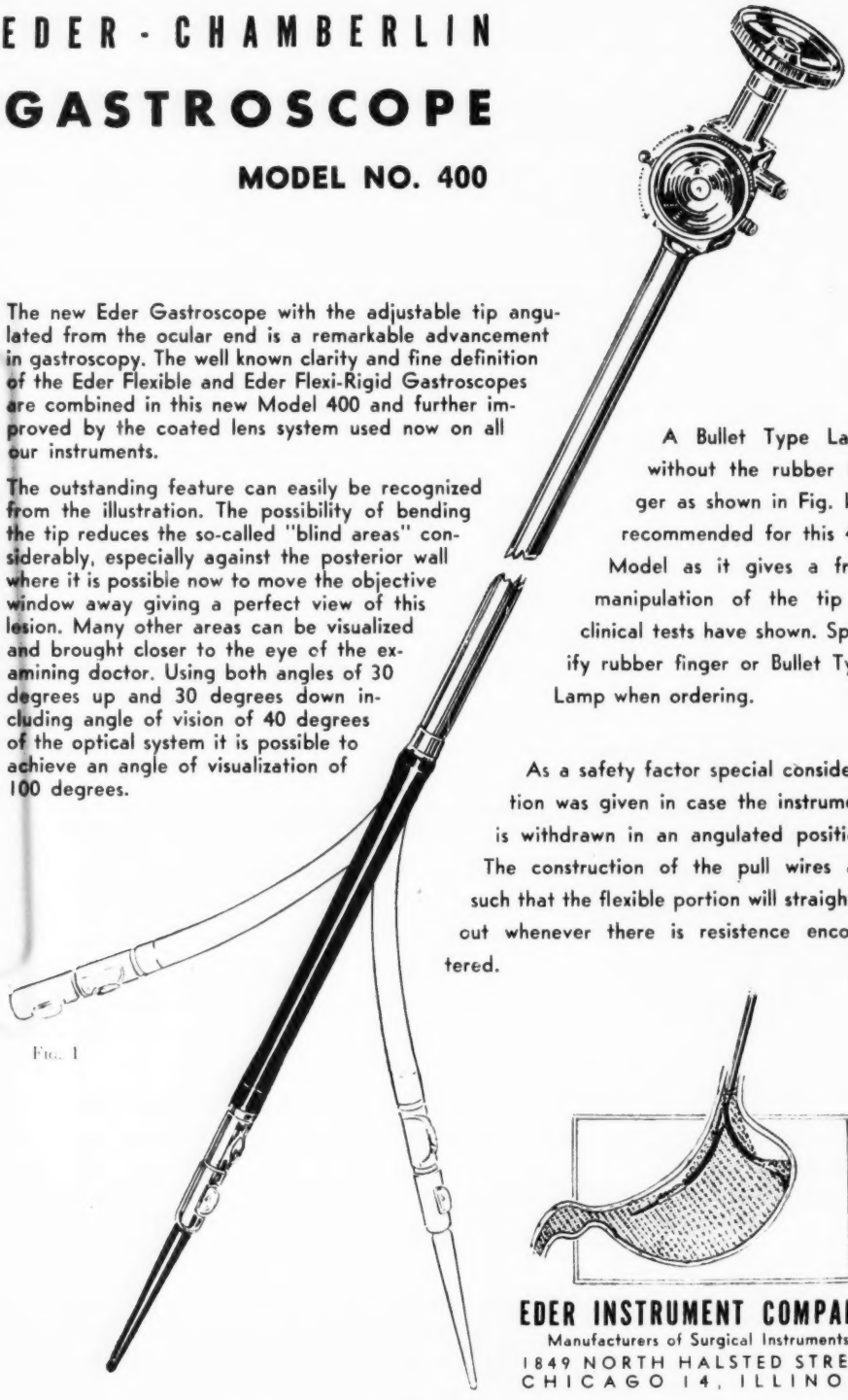


Fig. 1

A Bullet Type Lamp without the rubber finger as shown in Fig. 1, is recommended for this 400 Model as it gives a freer manipulation of the tip as clinical tests have shown. Specify rubber finger or Bullet Type Lamp when ordering.

As a safety factor special consideration was given in case the instrument is withdrawn in an angulated position. The construction of the pull wires are such that the flexible portion will straighten out whenever there is resistence encountered.

EDER INSTRUMENT COMPANY
Manufacturers of Surgical Instruments
1849 NORTH HALSTED STREET
CHICAGO 14, ILLINOIS

Faster healing in chronic ulcerative colitis and regional ileitis— CHLOROPHYLL THERAPY

In the treatment of intestinal diseases including ulcerative colitis, sigmoiditis, spastic colitis and regional ileitis, the basic advantages of chlorophyll therapy, as made possible by Chloresium Solution (Plain), represent a logical and optimistic approach to these major problems of the gastroenterologist.

Clinical improvement reported

Rafsky and Krieger* recently report definite improvement in the majority of cases in a series of twenty patients treated with Chloresium Solution (Plain). Their opinion was based not only on subjective clinical improvement, but also on careful proctoscopic, X-ray and sigmoidoscopic examinations.

Heals and deodorizes

Previous extensive laboratory and clinical studies have demonstrated the completely nontoxic, bland, healing qualities of the *water-soluble* derivatives of Chlorophyll "a" as supplied by Chloresium.

These natural biogenic agents accelerate normal cell regeneration, thus measurably hastening the healing process. At the same time, they help control superficial infection, provide symptomatic relief and deodorize foul-smelling suppurative conditions.

We invite you to try Chloresium Solution (Plain) by irrigation and instillation on your most resistant case of ulcerative colitis, regional ileitis or other gastroenterologic condition. Mail the coupon below for free clinical samples.

Accelerate healing. Stimulate normal cell growth. Control superficial infection. Reduce scar formation. Nontoxic, bland and soothing. Deodorize malodorous lesions.

Chloresium is ethically promoted
Available at leading druggists

Chloresium preparations contain the purified, therapeutically active *water-soluble* derivatives of Chlorophyll "a" ($C_{55}H_{72}O_5N_4Mg$). They are maintained to rigid chemical and physical standards and are pharmaceutically adjusted to a low surface tension to insure penetrability.

Chloresium
REG. U.S. PAT. OFF.

THERAPEUTIC CHLOROPHYLL PREPARATIONS

*Rafsky, H. and Krieger, C. L., The Treatment of Intestinal Diseases with Solutions of Water-Soluble Chlorophyll, (a preliminary report). Rev. Gastroenterology 15:549, 1948.

FREE! MAIL COUPON

RYSTAN COMPANY, INC., Dept. RG-2
7 N. MacQuesten Parkway,
Mount Vernon, New York

Please send reprint of paper by Rafsky and Krieger; "Chlorophyll—Its Use in Medicine," and clinical samples of Chloresium Solution (Plain) and Chloresium Ointment.

Name_____

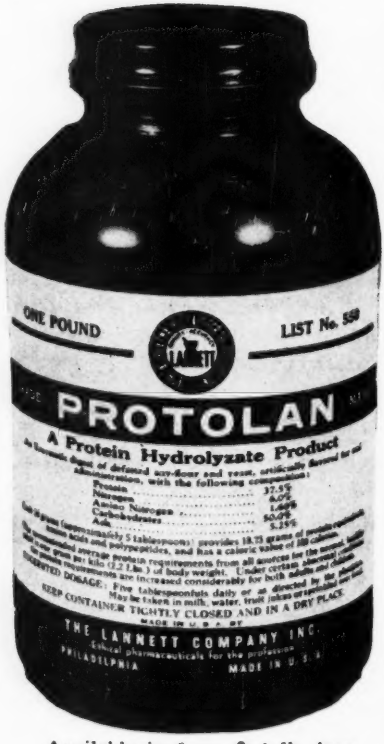
Street_____

City_____ Zone____ State____

IN THE TREATMENT OF PEPTIC ULCER*

PROTOLAN AFFORDS AN ORAL PROTEIN THAT **REALLY** IS

- **PALATABLE**
- **WELL-TOLERATED**
- **ECONOMICAL**



Available in 6 oz. & 1 lb. jars

PROTOLAN, the new Soya-Bean Protein Hydrolyzate, is an enzymatic digest of defatted Soya-Flour and Yeast, artificially flavored for oral administration. PROTOLAN supplies a full complement of the natural-occurring Amino acids and B-complex factors so essential to normal body maintenance and growth.

*FREE reprints available describing this new Protein Hydrolyzate and its use. Ask for article entitled "A New Protein Hydrolyzate for the Treatment of Peptic Ulcer".

Literature and clinical supplies upon request

Made in U. S. A. by

THE LANNETT COMPANY, INC.

Ethical Pharmaceuticals for the Profession

PHILADELPHIA 25, PA.

asymptomatic amebiasis

a major problem in public health

Non-dysenteric amebiasis is a major problem in control of infection with Endameba histolytica. This organism is harbored by about 13,000,000 people in the United States.* "Unfortunately, the necessity of treating asymptomatic patients is not generally realized in spite of the fact that these patients may develop acute symptoms at any time. *They excrete the infective cystic stage and spread the infection.*"**

Diagnosis depends on identification of the causative organism in stool specimens or its recovery from suspicious areas of intestinal mucosa by means of sigmoidoscopic aspiration.

ANAYODIN

(brand of chiniofon)

Bischoff

is speedily amebicidal in asymptomatic amebiasis – and the symptomatic form as well – destroying both cystic and trophozoite forms. Prompt and intensive treatment hastens healing of intestinal lesions.

ANAYODIN is relatively non-toxic, even in repeated courses.

A course of ANAYODIN therapy consists of 1 to 4 pills three times daily after meals for seven to fourteen days. Course may be repeated after ten-day interval.

ANAYODIN—Pills 0.25 Gm., in Bottles of 50 and 100

ANAYODIN—Powder, bottles of 25 and 100 Gm.

*Albrecht, F. K.: Modern Management in Clinical Medicine, Williams and Wilkins, Baltimore, 1940, p. 785.
**Ibid. p. 787

ERNST BISCHOFF COMPANY, INC · IVORYTON, CONNECTICUT

Protein Dietary in PEPTIC ULCER

Laboratory and clinical studies have shown the value of Knox unflavored Gelatine as an acid neutralizer, thus making it an effective inhibitor of gastric acidity and peptic activity.

Knox Gelatine, taken frequently in water, milk or fruit juices, helps control the gastric secretions and affords relief from painful symptoms. Unlike the ready-flavored gelatine powders with their high sugar and acid content, Knox unflavored Gelatine is *all* protein, thus supplementing an important factor frequently deficient in the diet of peptic ulcer patients.

"The Peptic Ulcer Dietary"

published by the Knox Gelatine Company, describes in detail the use of gelatine in the management of peptic ulcer. It is yours for the asking. Address Knox Gelatine, Dept. J 8, Johnstown, N. Y.

KNOX

Gelatine U.S.P.

ALL PROTEIN • NO SUGAR • NO FLAVORING

IN COMING ISSUES

Symposium on Ulcerative Colitis
Panel Discussion
Palliative Operation for
Gastric Cancer
Cancer of the Esophagus
Peptic Ulcer: Theory and Practice

In addition to other original articles, abstracts of current literature, editorials and book reviews.

Use convenient coupon below for insuring uninterrupted receipt of your copies.

Use this blank for subscribing to

The Review of Gastroenterology

1819 Broadway
New York 23, N. Y.

Enclosed please find $.....for which you are to enter my subscription to THE REVIEW OF GASTROENTEROLOGY, starting with the.....issue, as indicated below.

☐ **1 year $5.00** **($7.00 foreign)** ☐ **2 years $9.00** **($13.00 foreign)**

Name .....
(please print)

Address .....

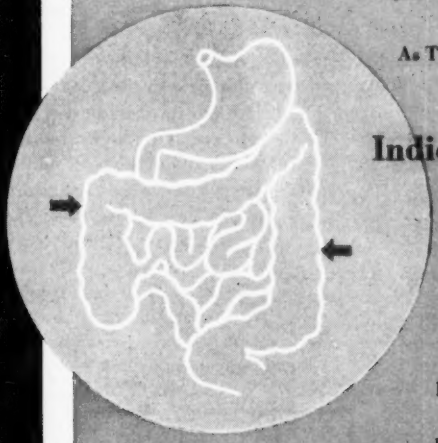
City ..... *Unit* ..... *State* .....

INTRODUCING:

Thalamyd

Phthalylsulfacetimide-Schering

THALAMYD,* a new "nonabsorbable" sulfonamide, for the treatment of enteric infections due to susceptible organisms and for preoperative prophylaxis in abdominal surgery, possesses the unique property of being absorbed by the intestinal mucosa in high concentration where it remains temporarily *without being absorbed by the blood stream in detectable amounts* following oral dosage. THALAMYD is bactericidal for common dysenteric organisms and for all coliform bacilli normally present in the intestine. THALAMYD, therefore, destroys susceptible pathogenic organisms within the *wall of the gut* as well as within its lumen. Because of its ability to temporarily *eliminate completely* E. coli from the intestinal flora,[1] it offers the latest approach to safer abdominal surgery.



As THALAMYD is virtually unabsorbed by the systemic circulation it is completely nontoxic to hematopoietic tissues and to the urinary tract.

Indications: Bacillary dysentery (shigellosis) and for preoperative prophylaxis in abdominal surgery. THALAMYD has proved effective in ulcerative colitis.[2]

dosage: 9 Gm. daily, in divided dosage, after meals. Usually, not more than 0.2 Gm. per kilogram of body weight is necessary in 24 hours. Children's dosage may be computed on this basis, up to 40 Kg. For ulcerative colitis higher dosages may be used without danger of toxicity, due to the nonabsorbable character of THALAMYD.

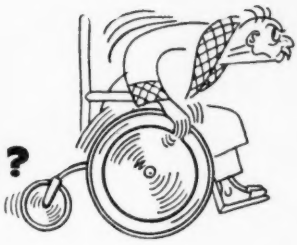
packaging: THALAMYD tablets contain 0.5 Gm. (7.7 gr.) of phthalylsulfacetimide per tablet. Bottles of 100 and 1000 tablets.

bibliography: 1. Sessera, H., and Henderson, F.: In press. 2. Heinsheimer, T., and Sessera, H.: Rev. Gastroenterol. *15*:611, 1948.

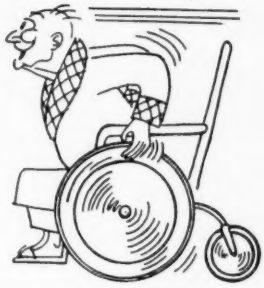
*THALAMYD trade-mark of Schering Corporation

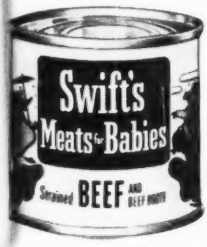
Schering CORPORATION • BLOOMFIELD, NEW JERSEY
IN CANADA, SCHERING CORPORATION LIMITED, MONTREAL

Sick folks sick of soft diets?



-try tempting Swift's Strained Meats!





6 varieties:
Beef, lamb, pork, veal, liver, heart

The foods soft-diet patients have to eat! No wonder they succumb to appetite-apathy.

But many physicians today have discovered there *is* a way to put appetizing, real meat goodness into soft diets. They recommend Swift's Strained Meats. These specially prepared meats retain all their palatability, and a maximum of nutrient value in a form that's highly digestible—easy to eat. To vary patients' menus, Swift's Strained Meats offer six different kinds: beef, lamb, pork, veal, liver, heart.

Nutritionally, Swift's Strained Meats provide an excellent base for a high-protein, low-residue diet. A rich source of complete, high-quality proteins, they make available simultaneously all known essential amino acids—for optimum protein synthesis. In addition, Swift's Strained Meats supply hemapoeitic iron and goodly amounts of B vitamins. They're convenient—ready to heat and serve. Let Swift's Strained Meats help overcome anorexia in your soft-diet patients!

The makers of Swift's Strained Meats invite you to send for the new physicians' handbook of protein feeding, written by a doctor, "The Importance of Protein Foods in Health and Disease." Send to:

SWIFT & COMPANY

Chicago 9, Illinois

ACCEPTED COUNCIL ON FOODS AND NUTRITION AMERICAN MEDICAL ASSOCIATION

All nutritional statements made in this advertisement are accepted by the Council on Foods and Nutrition of the American Medical Association.

For patients who can take foods of less fine consistency—Swift's Diced Meats offer tender morsels of nutritious meats with tempting flavors patients appreciate.

GASTRO-INTESTINAL NEUROSES

ALLIMIN Garlic Tablets are indicated as carminative medication for the relief of flatulent and nervous dyspepsia and many other gastro-intestinal neuroses.

Clinical studies have shown that ALLIMIN provides substantial relief of discomfort and heaviness after meals, belching, flatulence, gas colic and nausea. It is a useful palliative in the field of gastroenterology because it may be prescribed in a large variety of functional conditions which constitute the bulk of office practice.

ALLIMIN is the original garlic tablet recommended for use as a carminative. Each tablet contains 4-3/4 grains of dehydrated garlic, flavor modified with dried parsley and sugar-coated for palatability.

The recommended dose is 2 tablets after meals with a little water. Best results are obtained when the medication is continued three times daily. The tablets should be swallowed whole, not chewed.

ALLIMIN Garlic Tablets are available in cellophaned packages of 25, 60 and 250 tablets at all pharmacies.

Mail Coupon for Samples and Professional Literature

Allimin

The Safe and Effective Carminative for Long-Continued Use

VAN PATTEN PHARMACEUTICAL CO.
1227 Loyola Ave., Chicago, 26 RG 3-49

Gentlemen: Please send items checked:
☐ Covering Literature
☐ ALLIMIN Samples

Dr_____

Address_____

Town_____ State_____

Selective action

Selective antispasmodic action on the digestive tract and virtual freedom from side effects are outstanding advantages of Mesopin over belladonna and atropine. Thus, abdominal pain and discomfort due to spasticity and hypermotility can be effectively treated with increased specificity and greater safety. Supplied: Mesopin (2.5 mg. per tablet); available on prescription in bottles of 100 tablets. Samples sent on request.

brand of homatropine methyl bromide **Mesopin**

selective gastrointestinal antispasmodic

Endo Products Inc., Richmond Hill 18, N. Y.

Introducing..... ***Stigminene****

Bromide 'Warner'

The Newest Cholinergic Compound

Superior effects

Smooth balanced action

Minimum by-effects

WILLIAM R. WARNER & CO., INC. is proud to present STIGMINENE* BROMIDE 'Warner', an effective cholinergic compound of low toxicity, wide margin of therapeutic safety, and prolonged action.

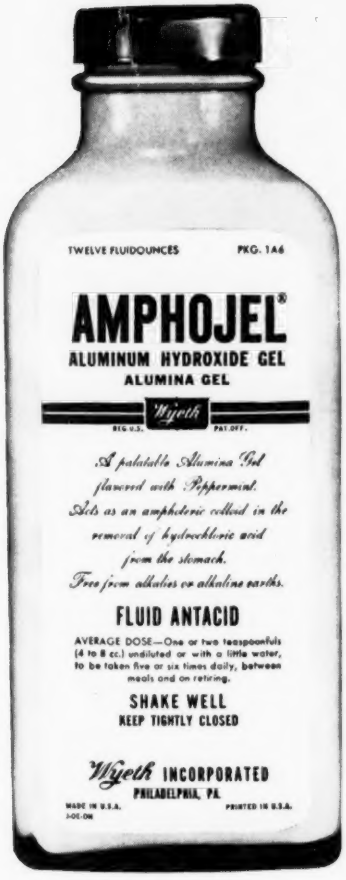
STIGMINENE* BROMIDE 'Warner' is indicated in the prevention and treatment of postoperative abdominal distention and urinary retention. It may be used for all degrees of intestinal and urinary bladder atony — from gastro-intestinal atony developing in chronic illness, certain acute infections or toxemias, and following anesthesia; meteorism complicating pneumonia; to as severe an involvement as paralytic ileus.

STIGMINENE* BROMIDE 'Warner' is supplied in 1-cc ampuls of a 1:2000 solution, 0.5 mg. each; cartons of 12 and 50 ampuls.

*Trade Mark

WILLIAM R. WARNER & CO., INC.

New York St. Louis



IN THE MEDICAL MANAGEMENT OF PEPTIC ULCER